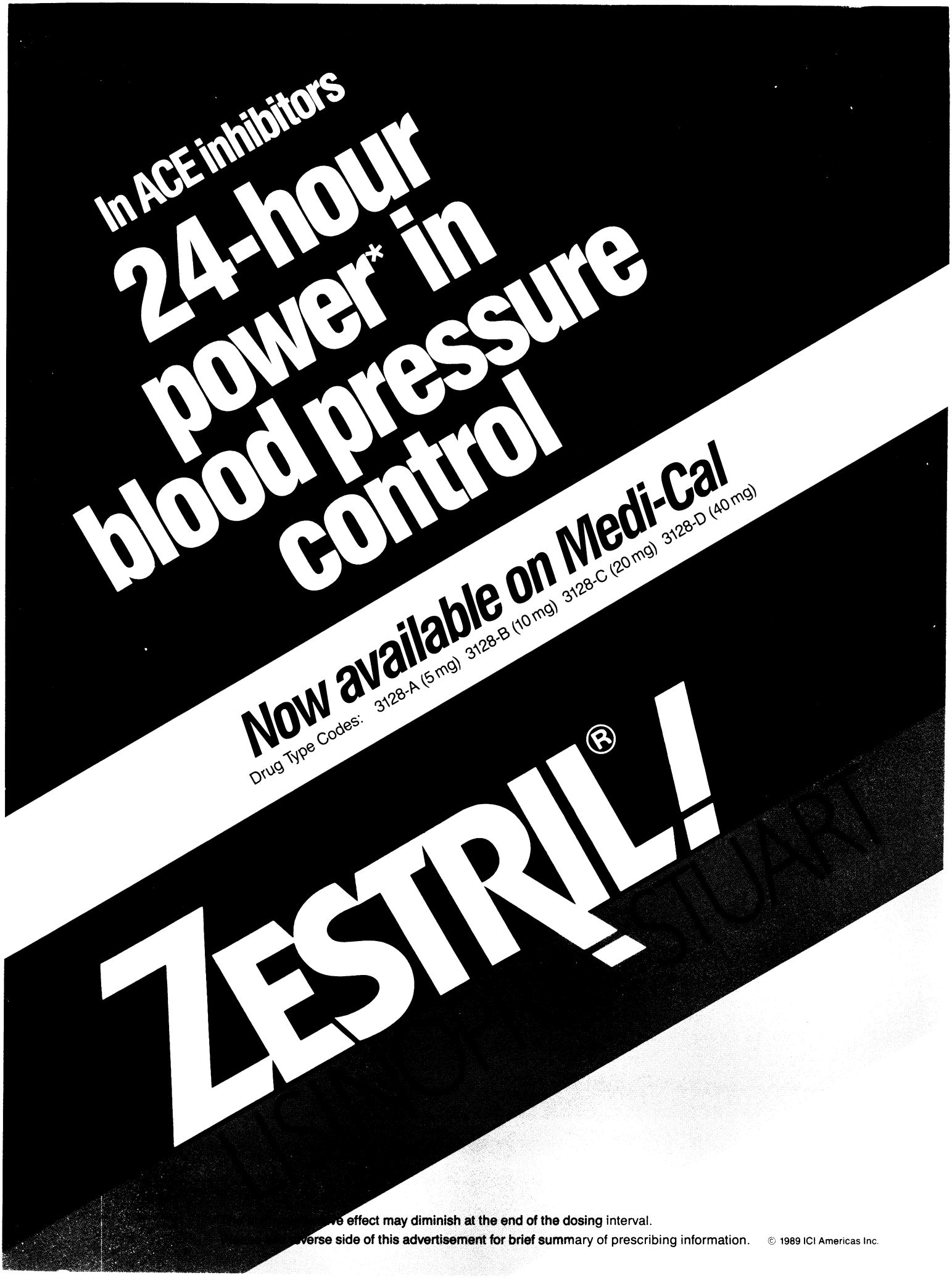

...e effect may diminish at the end of the dosing interval.

...verse side of this advertisement for brief summary of prescribing information.

INDICATIONS AND USAGE. ZESTRIL is indicated for the treatment of hypertension. It may be used alone as initial therapy or concomitantly with other classes of antihypertensive agents. In using ZESTRIL, consideration should be given to the fact that another angiotensin converting enzyme inhibitor, captopril, has caused agranulocytosis, particularly in patients with renal impairment or collagen vascular disease, and that available data are insufficient to show that ZESTRIL does not have a similar risk. (See WARNINGS.) **CONTRAINDICATIONS.** ZESTRIL is contraindicated in patients who are hypersensitive to this product and in patients with a history of angioedema related to previous treatment with an angiotensin converting enzyme inhibitor. **WARNINGS. Angioedema:** Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with angiotensin converting enzyme inhibitors, including ZESTRIL. In such cases, ZESTRIL should be promptly discontinued, and the patient carefully observed until the swelling disappears. In instances where swelling has been confined to the face and lips the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. **Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate therapy, eg, subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL) should be promptly administered. (See ADVERSE REACTIONS.) Hypotension:** Excessive hypotension was rarely seen in uncomplicated hypertensive patients but is a possible consequence of use with ZESTRIL in salt/volume-depleted persons, such as those treated vigorously with diuretics or patients on dialysis. (See PRECAUTIONS, Drug Interactions and ADVERSE REACTIONS.) In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed and may be associated with oliguria and/or progressive azotemia, and rarely with acute renal failure and/or death. Because of the potential fall in blood pressure in these patients, therapy should be started under very close medical supervision. Such patients should be followed closely for the first two weeks of treatment and whenever the dose of ZESTRIL and/or diuretic is increased. Similar considerations apply to patients with ischemic heart or cerebrovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident. If hypotension occurs, the patient should be placed in supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses which usually can be given without difficulty once the blood pressure has increased after volume expansion. **Neutropenia/Agranulocytosis:** Another angiotensin converting enzyme inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment especially if they also have a collagen vascular disease. Available data from clinical trials of ZESTRIL are insufficient to show that ZESTRIL does not cause agranulocytosis at similar rates. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered. **PRECAUTIONS. General. Impaired Renal Function:** As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe congestive heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with angiotensin converting enzyme inhibitors, including ZESTRIL, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death. In hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine may occur. Experience with another angiotensin converting enzyme inhibitor suggests that these increases are usually reversible upon discontinuation of ZESTRIL and/or diuretic therapy. In such patients, renal function should be monitored during the first few weeks of therapy. Some hypertensive patients with no apparent pre-existing renal vascular disease have developed increases in blood urea nitrogen and serum creatinine, usually minor and transient, especially when ZESTRIL has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction of ZESTRIL and/or discontinuation of the diuretic may be required. **Evaluation of the hypertensive patient should always include assessment of renal function. (See DOSAGE AND ADMINISTRATION.) Hyperkalemia:** In clinical trials hyperkalemia (serum potassium greater than 5.7 mEq/L) occurred in approximately 2.2% of hypertensive patients and 4.0% of patients with congestive heart failure. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in approximately 0.1% of hypertensive patients. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with ZESTRIL. (See Drug Interactions.) **Surgery/Anesthesia:** In patients undergoing major surgery or during anesthesia with agents that produce hypotension, ZESTRIL may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion. **Information for Patients. Angioedema:** Angioedema, including laryngeal edema, may occur especially following the first dose of ZESTRIL. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician. **Symptomatic Hypotension:** Patients should be cautioned to report lightheadedness especially during the first few days of therapy. If actual syncope occurs, the patient should be told to discontinue the drug until they have consulted with the prescribing physician. All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with their physician. **Hyperkalemia:** Patients should be told not to use salt substitutes containing potassium without consulting their physician. **Neutropenia:** Patients should be told to report promptly any indication of infection (eg, sore throat, fever) which may be a sign of neutropenia. **NOTE:** As with many other drugs, certain advice to patients being treated with ZESTRIL is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects. **DRUG INTERACTIONS. Hypotension – Patients on Diuretic Therapy:** Patients on diuretics and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with ZESTRIL. The possibility of hypotensive effects with ZESTRIL can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with ZESTRIL. If it is necessary to continue the diuretic, initiate therapy with ZESTRIL at a dose of 5 mg daily, and provide close medical supervision after the initial dose for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS, and DOSAGE AND ADMINISTRATION.) When a diuretic is added to the therapy of a patient receiving ZESTRIL, an additional antihypertensive effect is usually observed. Studies with ACE inhibitors in combination with diuretics indicate that the dose of the ACE inhibitor can be reduced when it is given with a diuretic. (See DOSAGE AND ADMINISTRATION.) **Indomethacin:** In a study in 36 patients with mild to moderate hypertension where the antihypertensive effects of ZESTRIL alone were compared to ZESTRIL given concomitantly with indomethacin, the use of indomethacin was associated with a reduced effect, although the difference between the two regimens was not significant. **Other Agents:** ZESTRIL has been used concomitantly with nitrates and/or digoxin without evidence of clinically significant adverse interactions. No clinically important pharmacokinetic interactions occurred when ZESTRIL was used concomitantly with propranolol or hydrochlorothiazide. The presence of food in the stomach does not alter the bioavailability of ZESTRIL. **Agents Increasing Serum Potassium:** ZESTRIL attenuates potassium loss caused by thiazide-type diuretics. Use of ZESTRIL with potassium-sparing diuretics (eg, spironolactone, triamterene or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. **Lithium:** Lithium toxicity has been reported in patients receiving lithium with drugs which cause elimination of sodium, including ACE inhibitors. Lithium toxicity was usually reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if ZESTRIL is administered concomitantly with lithium. **Carcinogenesis, Mutagenesis, Impairment of Fertility.** There was no evidence of a tumorigenic effect when lisinopril was administered for 105 weeks to male and female rats at doses up to 90 mg/kg/day (about 56 times* the maximum recommended daily human dose) or when lisinopril was administered for 92 weeks to (male and female) mice at doses up to 135 mg/kg/day (about 84 times* the maximum recommended daily human dose). *Based on patient weight of 50 kg. Lisinopril was not mutagenic in the Ames microbial mutagen test with or without metabolic activation. It was also negative in a forward mutation assay using Chinese hamster lung cells. Lisinopril did not produce single strand DNA breaks in an in vitro alkaline elution rat hepatocyte assay. In addition, lisinopril did not produce increases in chromosomal aberrations in an in vitro test in Chinese hamster ovary cells or in an in vivo study in mouse bone marrow. There were no adverse effects on reproductive performance in male and female rats treated with up to 300 mg/kg/day of lisinopril. **Pregnancy. Pregnancy Category C:** Lisinopril was not teratogenic in mice treated on days 6-15 of gestation with up to 1,000 mg/kg/day (625 times the maximum recommended human dose). There was an increase in fetal resorptions at doses down to 100 mg/kg; at doses of 1,000 mg/kg this was prevented by saline supplementation. There was no fetotoxicity or teratogenicity in rats treated with up to 300 mg/kg/day (188 times the maximum recommended dose) of lisinopril at days 6-17 of gestation. In rats receiving lisinopril from day 15 of gestation through day 21 postpartum, there was an increased incidence in pup deaths on days 2-7 postpartum and a lower average body weight of pups on day 21 postpartum. The increase in pup deaths and decrease in pup weight did not occur with maternal saline supplementation. Lisinopril, at doses up to 1 mg/kg/day, was not teratogenic when given throughout the organogenic period in saline supplemented rabbits. Saline supplementation (physiologic saline in place of tap water) was used to eliminate maternotoxic effects and enable evaluation of the teratogenic potential at the highest possible dosage level. The rabbit has been shown to be extremely sensitive to angiotensin converting enzyme inhibitors (captopril and enalapril) with maternal and fetotoxic effects apparent at or below the recommended therapeutic dosage levels in man. Fetotoxicity was demonstrated in rabbits by an increased incidence of fetal resorptions at an oral dose of lisinopril at 1 mg/kg/day and by an increased incidence of incomplete ossification at the lowest dose tested (0.1 mg/kg/day). A single intravenous dose of 15 mg/kg of lisinopril administered to pregnant rabbits on gestation days 16, 21 or 26 resulted in 88% to 100% fetal death. By whole body autoradiography, radioactivity was found in the placenta following administration of labeled lisinopril to pregnant rats, but none was found in the fetuses. **Human Experience:** There are no adequate and well-controlled studies of lisinopril in pregnant women. However, data are available that show drugs of this class cross the human placenta. Because the risk of fetal toxicity with the use the ACE inhibitors has not been clearly defined (see below), lisinopril should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Postmarketing experience with all ACE inhibitors thus far suggests the following with regard to pregnancy outcome. Inadvertent exposure limited to the first trimester of pregnancy has not been reported to affect fetal outcome adversely. Fetal exposure during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality. When ACE inhibitors are used during the later stages of pregnancy, there have been reports of hypotension and decreased renal perfusion in the newborn. Oligohydramnios in the mother has also been reported, presumably representing decreased renal function in the fetus. Infants exposed in utero to ACE inhibitors should be closely observed for hypotension, oliguria and hyperkalemia. If oliguria occurs, attention should be directed toward

ZESTRIL® (lisinopril)

support of blood pressure and renal perfusion with the administration of fluids and pressores as appropriate. Problems associated with prematurity such as patent ductus arteriosus have occurred in association with maternal use of ACE inhibitors, but it is not clear whether they are related to ACE inhibition, maternal hypertension or the underlying prematurity. Another ACE inhibitor, enalapril, has been removed from the neonatal circulation by peritoneal dialysis and theoretically may be removed by exchange transfusion, although there is no experience with the latter procedure. There is no experience with either of these procedures for removing lisinopril or other ACE inhibitors from the neonatal circulation. **Nursing Mothers:** Milk of lactating rats contains radioactivity following administration of ^{14}C lisinopril. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ZESTRIL is given to a nursing mother. **Pediatric Use:** Safety and effectiveness in children have not been established. **ADVERSE REACTIONS.** ZESTRIL has been found to be generally well tolerated in controlled clinical trials involving 2003 patients and subjects. The most frequent clinical adverse experiences in controlled trials with ZESTRIL were dizziness (6.3%), headache (5.3%), fatigue (3.3%), diarrhea (3.2%), upper respiratory symptoms (3.0%), and cough (2.9%), all of which were more frequent than in placebo-treated patients. For the most part, adverse experiences were mild and transient in nature. Discontinuation of therapy was required in 6.0% of patients. In clinical trials, the overall frequency of adverse experiences could not be related to total daily dosage within the recommended therapeutic dosage range. For adverse experiences which occurred in more than 1% of patients and subjects treated with ZESTRIL or ZESTRIL plus hydrochlorothiazide in controlled clinical trials, comparative incidence data are listed in the table below.

Percent of Patients in Controlled Studies

	ZESTRIL (n = 2003†) Incidence (discontinuation)	ZESTRIL/Hydrochlorothiazide (n = 644) Incidence (discontinuation)	Placebo (n = 207) Incidence
Dizziness	6.3 (0.6)	9.0 (0.9)	1.9
Headache	5.3 (0.2)	4.3 (0.5)	1.9
Fatigue	3.3 (0.2)	3.9 (0.5)	1.0
Diarrhea	3.2 (0.3)	2.6 (0.3)	2.4
Upper Respiratory Symptoms	3.0 (0.0)	4.5 (0.0)	0.0
Cough	2.9 (0.4)	4.5 (0.8)	1.0
Nausea	2.3 (0.3)	2.5 (0.2)	2.4
Hypotension	1.8 (0.8)	1.6 (0.5)	0.5
Rash	1.5 (0.4)	1.6 (0.2)	0.5
Orthostatic Effects	1.4 (0.0)	3.4 (0.2)	1.0
Asthenia	1.3 (0.4)	2.0 (0.2)	1.0
Chest Pain	1.3 (0.1)	1.2 (0.2)	1.4
Vomiting	1.3 (0.2)	1.4 (0.0)	0.5
Dyspnea	1.1 (0.0)	0.5 (0.2)	1.4
Dyspepsia	1.0 (0.0)	1.9 (0.0)	0.0
Paresthesia	0.8 (0.0)	2.0 (0.2)	0.0
Impotence	0.7 (0.2)	1.6 (0.3)	0.0
Muscle Cramps	0.6 (0.0)	2.8 (0.6)	0.5
Back Pain	0.5 (0.0)	1.1 (0.0)	1.4
Nasal Congestion	0.3 (0.0)	1.2 (0.0)	0.0
Decreased Libido	0.2 (0.1)	1.2 (0.0)	0.0
Vertigo	0.1 (0.0)	1.1 (0.2)	0.0

†Includes 420 patients treated for congestive heart failure who were receiving concomitant digitalis and/or diuretic therapy.

Clinical adverse experiences occurring in 0.3% to 1.0% of patients in the controlled trials and rarer, serious, possibly drug related events reported in uncontrolled studies or marketing experience included: BODY AS A WHOLE: Chest discomfort, fever, flushing. CARDIOVASCULAR: Angina pectoris, orthostatic hypotension, rhythm disturbances, tachycardia, peripheral edema, palpitation. DIGESTIVE: Abdominal pain, anorexia, constipation, flatulence. METABOLISM: Gout. MUSCULOSKELETAL: Joint pain, shoulder pain. NERVOUS SYSTEM/PSYCHIATRIC: Depression, somnolence, insomnia, stroke. RESPIRATORY SYSTEM: Bronchitis, sinusitis, pharyngeal pain. UROGENITAL: Oliguria, progressive azotemia, acute renal failure. OTHER: Blurred vision, pruritus, urinary tract infection, vasculitis of the legs. ANGIOEDEMA: Angioedema has been reported in patients receiving ZESTRIL (0.1%). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis and/or larynx occurs, treatment with ZESTRIL should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.) HYPOTENSION: In hypertensive patients, hypotension occurred in 1.2% and syncope occurred in 0.1% of patients. Hypotension or syncope was a cause of discontinuation of therapy in 0.5% of hypertensive patients. (See WARNINGS.) In patients with congestive heart failure, hypotension occurred in 5.0% and syncope occurred in 1.0% of patients. These adverse experiences were causes for discontinuation of therapy in 1.3% of these patients. **Clinical Laboratory Test Findings. Serum Electrolytes:** Hyperkalemia. (See PRECAUTIONS.) **Creatinine, Blood Urea Nitrogen:** Minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 2.0% of patients with essential hypertension treated with ZESTRIL alone. Increases were more common in patients receiving concomitant diuretics and in patients with renal artery stenosis. (See PRECAUTIONS.) Reversible minor increases in blood urea nitrogen and serum creatinine were observed in approximately 9.1% of patients with congestive heart failure on concomitant diuretic therapy. Frequently, these abnormalities resolved when the dosage of the diuretic was decreased. **Hemoglobin and Hematocrit:** Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.4 g% and 1.3 vol%, respectively) occurred frequently in patients treated with ZESTRIL but were rarely of clinical importance in patients without some other cause of anemia. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia. **Other (Causal Relationship Unknown):** Rarely, elevations of liver enzymes and/or serum bilirubin have occurred. Overall, 2.0% of patients discontinued therapy due to laboratory adverse experiences, principally elevations in blood urea nitrogen (0.6%), serum creatinine (0.5%), and serum potassium (0.4%). **OVERDOSAGE.** The oral LD_{50} of lisinopril is greater than 20 g/kg in mice and rats. The most likely manifestation of overdosage would be hypotension, for which the usual treatment would be intravenous infusion of normal saline solution. Lisinopril can be removed by hemodialysis. **DOSAGE AND ADMINISTRATION. Initial Therapy:** In patients with uncomplicated essential hypertension not on diuretic therapy, the recommended initial dose is 10 mg once a day. Dosage should be adjusted according to blood pressure response. The usual dosage range is 20-40 mg per day administered in a single daily dose. The antihypertensive effect may diminish toward the end of the dosing interval regardless of the administered dose, but most commonly with a dose of 10 mg daily. This can be evaluated by measuring blood pressure just prior to dosing to determine whether satisfactory control is being maintained for 24 hours. If it is not, an increase in dose should be considered. Doses up to 80 mg have been used but do not appear to give greater effect. If blood pressure is not controlled with ZESTRIL alone, a low dose of a diuretic may be added. Hydrochlorothiazide, 12.5 mg has been shown to provide an additive effect. After the addition of a diuretic, it may be possible to reduce the dose of ZESTRIL. **Diuretic Treated Patients:** In hypertensive patients who are currently being treated with a diuretic, symptomatic hypotension may occur occasionally following the initial dose of ZESTRIL. The diuretic should be discontinued, if possible, for two to three days before beginning therapy with ZESTRIL to reduce the likelihood of hypotension. (See WARNINGS.) The dosage of ZESTRIL should be adjusted according to blood pressure response. If the patient's blood pressure is not controlled with ZESTRIL alone, diuretic therapy may be resumed as described above. If the diuretic cannot be discontinued, an initial dose of 5 mg should be used under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS and PRECAUTIONS, Drug Interactions.) Concomitant administration of ZESTRIL with potassium supplements, potassium salt substitutes, or potassium-sparing diuretics may lead to increases of serum potassium. (See PRECAUTIONS.) **Use in Elderly:** In general, blood pressure response and adverse experiences were similar in younger and older patients given similar doses of ZESTRIL. Pharmacokinetic studies, however, indicate that maximum blood levels and area under the plasma concentration time curve (AUC) are doubled in older patients so that dosage adjustments should be made with particular caution. **Dosage Adjustment in Renal Impairment:** The usual dose of ZESTRIL (10 mg) is recommended for patients with creatinine clearance > 30 mL/min (serum creatinine of up to approximately 3 mg/dL). For patients with creatinine clearance ≥ 10 mL/min ≤ 30 mL/min (serum creatinine ≥ 3 mg/dL), the first dose is 5 mg once daily. For patients with creatinine clearance < 10 mL/min (usually on hemodialysis) the recommended initial dose is 2.5 mg. The dosage may be titrated upward until blood pressure is controlled or to a maximum of 40 mg daily.

Renal Status	Creatinine Clearance mL/min	Initial Dose mg/day
Normal Renal Function to Mild Impairment	>30	10
Moderate to Severe Impairment	≥ 10 ≤ 30	5
Dialysis Patients	< 10	2.5‡

‡Dosage or dosing interval should be adjusted depending on the blood pressure response.

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The following is a brief summary only. Before prescribing, see complete prescribing information in Tenex product labeling.

Contraindications: Tenex is contraindicated in patients with known hypersensitivity to guanfacine hydrochloride.

Precautions: *General.* Like other antihypertensive agents, Tenex (guanfacine hydrochloride) should be used with caution in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease or chronic renal or hepatic failure.

Sedation. Tenex, like other orally active central alpha-2 adrenergic agonists, causes sedation or drowsiness, especially when beginning therapy. These symptoms are dose-related (see Adverse Reactions). When Tenex is used with other centrally active depressants (such as phenothiazines, barbiturates, or benzodiazepines), the potential for additive sedative effects should be considered.

Rebound. Abrupt cessation of therapy with orally active central alpha-2 adrenergic agonists may be associated with increases (from depressed on-therapy levels) in plasma and urinary catecholamines, symptoms of "nervousness and anxiety" and, less commonly, increases in blood pressure to levels significantly greater than those prior to therapy.

Information for Patients. Patients who receive Tenex should be advised to exercise caution when operating dangerous machinery or driving motor vehicles until it is determined that they do not become drowsy or dizzy from the medication. Patients should be warned that their tolerance for alcohol and other CNS depressants may be diminished. Patients should be advised not to discontinue therapy abruptly.

Laboratory Tests. In clinical trials, no clinically relevant laboratory test abnormalities were identified as causally related to drug during short-term treatment with Tenex (guanfacine hydrochloride).

Drug Interactions. No specific adverse drug interactions have been identified, but the potential for increased sedation when Tenex is given with other CNS-depressant drugs should be appreciated.

Anticoagulants. Ten patients who were stabilized on oral anticoagulants were given guanfacine, 1–2 mg/day, for 4 weeks. No changes were observed in the degree of anticoagulation.

In several well-controlled studies, guanfacine was administered together with diuretics with no drug interactions reported. In the long-term safety studies, Tenex was given concomitantly with many drugs without evidence of any interactions. The principal drugs given (number of patients in parentheses) were: cardiac glycosides (115), sedatives and hypnotics (103), coronary vasodilators (52), oral hypoglycemics (45), cough and cold preparations (45), NSAIDs (38), antihyperlipidemics (29), antigout drugs (24), oral contraceptives (18), bronchodilators (13), insulin (10), and beta blockers (10).

Drug/Laboratory Test Interactions. No laboratory test abnormalities related to the use of Tenex (guanfacine hydrochloride) have been identified.

Carcinogenesis, Mutagenesis, Impairment of Fertility. No carcinogenic effect was observed in studies of 78 weeks in mice at doses more than 150 times the maximum recommended human dose and 102 weeks in rats at doses more than 100 times the maximum recommended human dose. In a variety of test models guanfacine was not mutagenic.

No adverse effects were observed in fertility studies in male and female rats.

Pregnancy Category B. Administration of guanfacine to rats at 70 times the maximum recommended human dose and rabbits at 20 times the maximum recommended human dose resulted in no evidence of impaired fertility or harm to the fetus. Higher doses (100 and 200 times the maximum recommended human dose in rabbits and rats respectively) were associated with reduced fetal survival and maternal toxicity. Rat experiments have shown that guanfacine crosses the placenta.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery. Tenex (guanfacine hydrochloride) is not recommended in the treatment of acute hypertension associated with toxemia of pregnancy. There is no information available on the effects of guanfacine on the course of labor and delivery.

Nursing Mothers. It is not known whether Tenex (guanfacine hydrochloride) is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Tenex is administered to a nursing woman. Experiments with rats have shown that guanfacine is excreted in the milk.

Pediatric Use. Safety and effectiveness in children under 12 years of age have not been demonstrated. Therefore, the use of Tenex in this age group is not recommended.

Adverse Reactions: Adverse reactions noted with Tenex (guanfacine hydrochloride) are similar to those of other drugs of the central α-2 adrenoreceptor agonist class: dry mouth, sedation (somnolence), weakness (asthenia), dizziness, constipation, and impotence. While the reactions are common, most are mild and tend to disappear on continued dosing.

Skin rash with exfoliation has been reported in a few cases; although clear cause and effect relationships to Tenex could not be established, should a rash occur, Tenex should be discontinued and the patient monitored appropriately.

In a 12-week placebo-controlled, dose-response study the frequency of the most commonly observed adverse reactions showed a clear dose relationship from 0.5 to 3 mg, as follows:

Adverse Reaction	Assigned Treatment Group				
	Placebo	0.5 mg	1.0 mg	2.0 mg	3.0 mg
n=	73	72	72	72	72
Dry Mouth	5 (7%)	4 (5%)	6 (8%)	8 (11%)	20 (28%)
Somnolence	1 (1%)	3 (4%)	0 (0%)	1 (1%)	10 (14%)
Asthenia	0 (0%)	2 (3%)	0 (0%)	2 (2%)	7 (10%)
Dizziness	2 (2%)	1 (1%)	3 (4%)	6 (8%)	3 (4%)
Headache	3 (4%)	4 (3%)	3 (4%)	1 (1%)	2 (2%)
Impotence	1 (1%)	1 (1%)	0 (0%)	1 (1%)	3 (4%)
Constipation	0 (0%)	0 (0%)	0 (0%)	1 (1%)	1 (1%)
Fatigue	3 (3%)	2 (3%)	2 (3%)	5 (6%)	3 (4%)

There were 41 premature terminations because of adverse reactions in this study. The percent of patients who terminated and the dose at which they terminated were as follows:

Dose:	Placebo	0.5 mg	1 mg	2 mg	3 mg
Terminated:	6.9%	4.2%	3.2%	6.9%	8.3%

Reasons for dropouts among patients who received guanfacine were: somnolence, headache, weakness, dry mouth, dizziness, impotence, insomnia, constipation, syncope, urinary incontinence, conjunctivitis, paresthesia, and dermatitis.

In a second placebo-controlled study in which the dose could be adjusted upward to 3 mg per day in 1-mg increments at 3-week intervals, i.e., a setting more similar to ordinary clinical use, the most commonly recorded reactions were: dry mouth 47%, constipation 16%, fatigue 12%, somnolence 10%, asthenia 6%, dizziness 6%, headache 4%, and insomnia 4%.

Reasons for dropouts among patients who received guanfacine were: somnolence, dry mouth, dizziness, impotence, constipation, confusion, depression, and palpitations.

In the clonidine/guanfacine comparison described in Clinical Pharmacology, the most common adverse reactions noted were:

	Guanfacine (n = 279)	Clonidine (n = 278)
Dry mouth	30%	37%
Somnolence	21%	35%
Dizziness	11%	8%
Constipation	10%	5%
Fatigue	9%	8%
Headache	4%	4%
Insomnia	4%	3%

Adverse reactions occurring in 3% or less of patients in the three controlled trials were:

Cardiovascular—	bradycardia, palpitations, substernal pain
Gastrointestinal—	abdominal pain, diarrhea, dyspepsia, dysphagia, nausea
CNS—	amnesia, confusion, depression, insomnia, libido decrease
ENT disorders—	rhinitis, taste perversion, tinnitus
Eye disorders—	conjunctivitis, iritis, vision disturbance
Musculoskeletal—	leg cramps, hypokinesia
Respiratory—	dyspnea
Dermatologic—	dermatitis, pruritus, purpura, sweating
Urogenital—	testicular disorder, urinary incontinence
Other—	malaise, paresthesia, paresis

Adverse reaction reports tend to decrease over time. In an open-label trial of one year's duration, 580 hypertensive subjects were given guanfacine, titrated to achieve goal blood pressure, alone (51%), with diuretic (38%), with beta blocker (3%), with diuretic plus beta blocker (6%), or with diuretic plus vasodilator (2%). The mean daily dose of guanfacine reached was 4.7 mg.

Adverse Reaction	Incidence of adverse reactions at any time during the study	Incidence of adverse reactions at end of one year
N	580	580
Dry mouth	60%	15%
Drowsiness	33%	6%
Dizziness	15%	1%
Constipation	14%	3%
Weakness	5%	1%
Headache	4%	0.2%
Insomnia	5%	0%

There were 52 (8.9%) dropouts due to adverse effects in this 1-year trial. The causes were: dry mouth (n = 20), weakness (n = 12), constipation (n = 7), somnolence (n = 3), nausea (n = 3), orthostatic hypotension (n = 2), insomnia (n = 1), rash (n = 1), nightmares (n = 1), headache (n = 1), and depression (n = 1).

Rev. May 1988

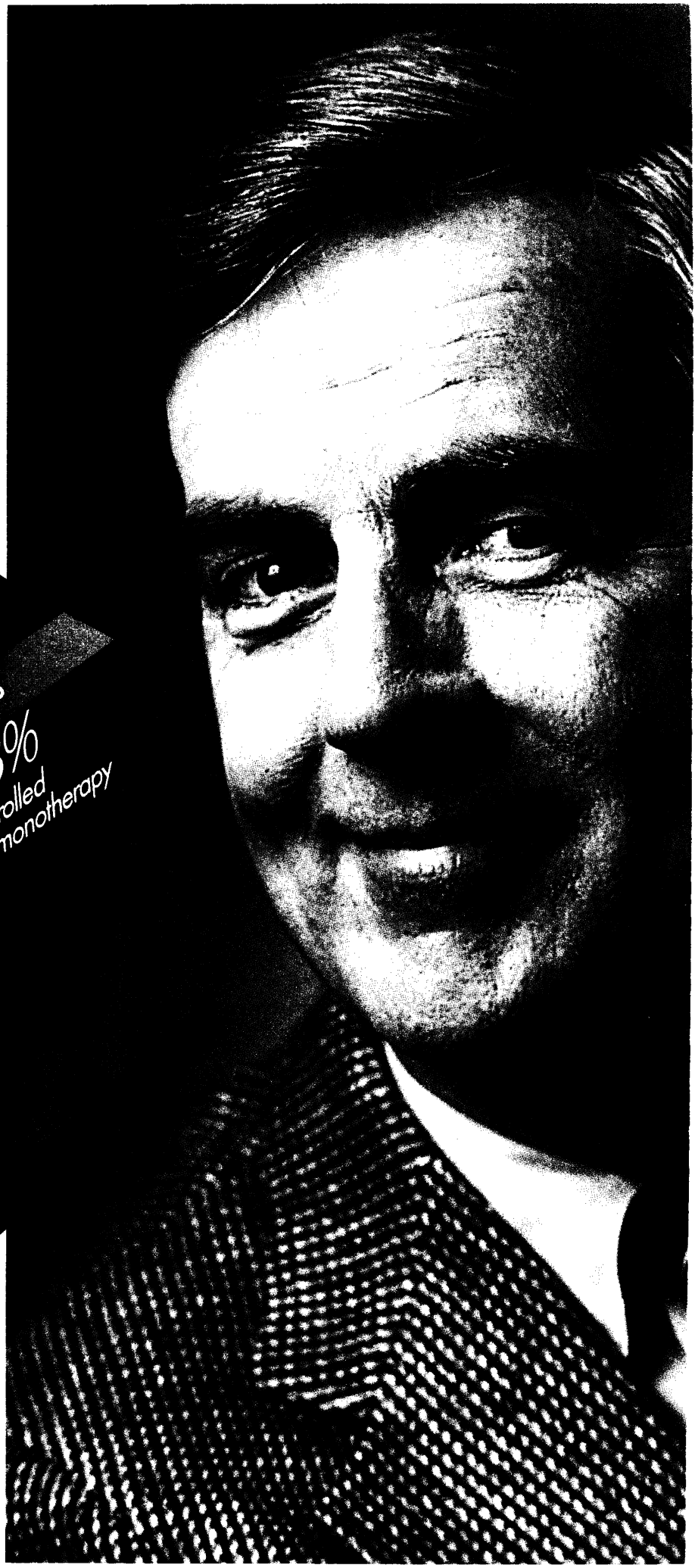
A.H. Robins Company 1988 Richmond, Virginia 23261-6609

Initial monotherapy regardless of age* or race

Therapeutic goal achieved in more than 80% of patients with mild-to-moderate hypertension[1†‡]

Study A
82%

Study B
83%
Controlled with monotherapy



*For adult hypertensives only.

†Eighty-two percent of 3,604 patients with mild-to-moderate hypertension (30–70 years) achieved goal blood pressure (DBP ≤ 90 mm Hg) in an open, multicenter, six-week study.

‡In a double-blind, forced dose titration comparative study of 394 black patients with mild-to-moderate hypertension (18–70 years), 83% of those randomized to Calan SR (n = 54) at a dosage of 360 mg/day achieved goal blood pressure (DBP < 90 mm Hg or > 10 mm Hg reduction).

Once-a-day antihypertensive monotherapy

- Calan SR provides effective monotherapy in more than 80% of all adult patients.[1]
- 91% of patients take Calan SR once a day[1]—a more convenient dosage schedule that may result in better compliance than twice-daily therapy.[2]
- Calan SR is equally effective in black and white adult patients, regardless of age.[1]
- Physicians have demonstrated their confidence in Calan SR—more than 12 million prescriptions have been filled.

One agent...for quality living

- Improved or maintained quality of life was reported by 400 hypertensive patients on Calan SR in two double-blind, controlled clinical studies.[1,3]

Constipation, which can be easily managed in most patients, is the most commonly reported side effect with Calan SR.

Please see the following page of this advertisement for references and a brief summary of the complete prescribing information.

Calan

(verapamil HCl) 240mg

SUSTAINED-RELEASE **CAPLETS**

Inconceivable? Not at all.

Is there any way you can get **good** patient accounting software for a **reasonable price?**

Yes there is... with MediSoft Patient Accounting!

With **over 2400 systems in use,** MediSoft Patient Accounting has earned a reputation as the value leader in healthcare software. MediSoft's extraordinarily low price is *unheard of* in the healthcare software industry where most software sells for *over ten times the price.*

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- Aging Reports
- Statements
- Daysheet
- Practice Analysis
- Transaction Journal
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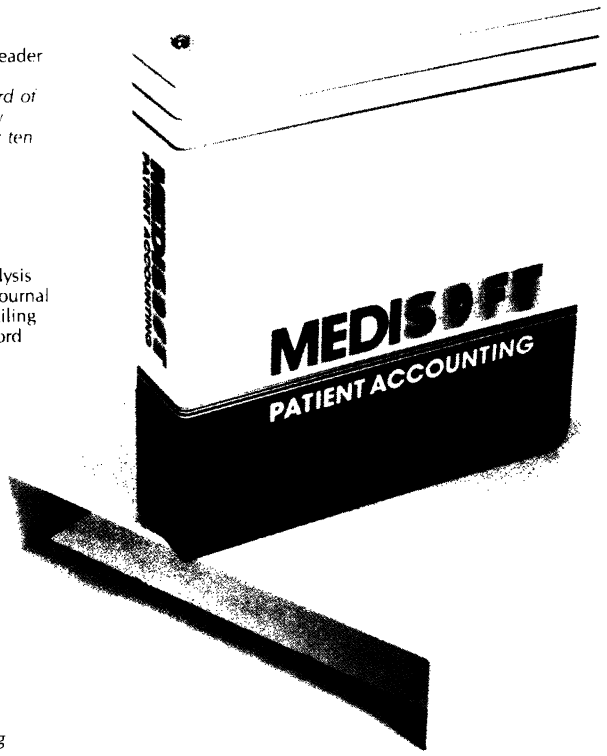

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- Insurance Aging Report
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- Aging reports designed for use as a collection worksheet

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EXPERT Advice
Our full-time technical support staff is only a phone call away. Our experienced technicians answer your questions quickly and accurately.

"The Medisoft Patient Accounting program is easy to install and learn, and is inexpensive enough for any medical practitioner to use. I wish MediSoft had been around sooner."
Brent W. Davis, D.O.

"I had some good personal experience with a low priced accounting software package and I was convinced that you could pay a low price and still get a good program."
Tyron Girod, M.D.

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Optional Electronic Insurance Claim Submission:
Billing data is transferred from MediSoft Patient Accounting for submission of insurance claims with an ordinary 1200 or 2400 baud modem. Medicare, Medicaid, commercial and Blue Cross/Blue Shield carriers are supported.

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Batik painting
by Wiji Hartono/Kabul,
Yogyakarta, Indonesia

Educational Program

The 1990 program will focus on emergency medicine, cardiovascular disease, and obstetrics and gynecology. Faculty will be from the University of Minnesota Medical School. In addition presentations and demonstrations will be given by Indonesian physicians and healers, and we will tour a general hospital in Bali. The Yogyakarta extension includes a visit to a community clinic and to a private Moslem hospital.

Indonesia

In addition to its beautiful beaches, Bali's attractions include its fascinating Hindu culture, volcanic mountains, terraced rice paddies, busy markets, and many craft shops. Yogyakarta, long the arts center of Indonesia, is an excellent example of the eclectic Moslem culture of Central Java.

Bali Tour Includes

• Roundtrip airfare from Los Angeles to Bali via Garuda Indonesia Airlines • Seven nights accommodation at the Sanur Beach Hotel, Bali • American breakfast daily, welcome and farewell dinners • Two half-day tours: Besakih Temple, Tanah Lot, Monkey Forest, Ubud, and Mas • Roundtrip transfers • Porterage and hospitality desk at the Sanur Beach Hotel

Optional Extension to Yogyakarta (2/25-28)

• Roundtrip airfare from Bali • Three nights accommodation at the Puri Artha Cottages • City tour • Visit to Borobudur, largest Buddhist temple in the world • Clinic and hospital visits • Optional dinner at Sultan's Palace

Cost Summary

Total land and air from Los Angeles (per person, double occupancy) $1595
Yogyakarta extension (per person, double occupancy) $ 215

For Further Information

Office of Continuing Medical Education, Continuing Education and Extension, Box 202, UMHC, 420 Delaware St. S.E., Minneapolis, MN 55455; telephone 612-626-5525; FAX 612-626-4411. Bart Galle, PhD, Director, 612-626-4046 • Group Travel Directors: outside Minnesota 1-800-222-7907; Telex 4950462; FAX 612-881-6276

The benefit of antianginal protection plus safety...

CARDIZEM®: A FULLER LIFE

diltiazem HCl/Marion

60 mg 90/120 mg GREATER DOSAGE FLEXIBILITY

***A remarkable safety profile*[1-6]**

The low incidence of side effects with Cardizem allows patients to feel better.

***Protection against angina attacks*[1,5,7-9]**

The predictable efficacy of Cardizem in stable exertional and vasospastic angina allows patients to do more.*

A decrease in myocardial oxygen demand

Resulting from a lowered heart rate-blood pressure product.[5]

***Compatible with other antianginals*[6†]**

***Safe in angina with coexisting hypertension, COPD, asthma, or PVD*[1,3,5,6]**

**CARDIZEM® (diltiazem HCl) is indicated in the treatment of angina pectoris due to coronary artery spasm and in the management of chronic stable angina (classic effort-associated angina) in patients who cannot tolerate therapy with beta-blockers and/or nitrates or who remain symptomatic despite adequate doses of these agents.*

†See Warnings and Precautions.

Please see brief summary of prescribing information on the next page.

1419H8

CARDIZEM® ANTIANGINAL PROTECTION PLUS SAFETY

diltiazem HCl/Marion

Usual maintenance dosage range: 180-360 mg/day

BRIEF SUMMARY
Professional Use Information

CARDIZEM®
(diltiazem HCl)
30 mg, 60 mg, 90 mg and 120 mg Tablets

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, (3) patients with hypotension (less than 90 mm Hg systolic), (4) patients who have demonstrated hypersensitivity to the drug, and (5) patients with acute myocardial infarction and pulmonary congestion documented by x-ray on admission.

WARNINGS

1. ***Cardiac Conduction.*** *CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.*
2. ***Congestive Heart Failure.*** *Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.*
3. ***Hypotension.*** *Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.*
4. ***Acute Hepatic Injury.*** *In rare instances, significant elevations in enzymes such as alkaline phosphatase, LDH, SGOT, SGPT, and other phenomena consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)*

PRECAUTIONS

General. *CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.*

Dermatological events (see ADVERSE REACTIONS section) may be transient and may disappear despite continued use of CARDIZEM. However, skin eruptions progressing to erythema multiforme and/or exfoliative dermatitis have also been infrequently reported. Should a dermatologic reaction persist, the drug should be discontinued.

Drug Interaction. *Due to the potential for additive effects, caution and careful titration are warranted in patients receiving CARDIZEM concomitantly with any agents known to affect cardiac contractility and/or conduction. (See WARNINGS.)*

Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

As with all drugs, care should be exercised when treating patients with multiple medications. CARDIZEM undergoes biotransformation by cytochrome P-450 mixed function oxidase. Coadministration of CARDIZEM with other agents which follow the same route of biotransformation may result in the competitive inhibition of metabolism. Dosages of similarly metabolized drugs, particularly those of low therapeutic ratio or in patients with renal and/or hepatic impairment, may require adjustment when starting or stopping concomitantly administered CARDIZEM to maintain optimum therapeutic blood levels.

Beta-blockers: *Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities.*

Administration of CARDIZEM (diltiazem hydrochloride) concomitantly with propranolol in five normal volunteers resulted in increased propranolol levels in all subjects and bioavailability of propranolol was increased approximately 50%. If combination therapy is initiated or withdrawn in conjunction with propranolol, an adjustment in the propranolol dose may be warranted. (See WARNINGS.)

Cimetidine: *A study in six healthy volunteers has shown a significant increase in peak diltiazem plasma levels (58%) and area-under-the-curve (53%) after a one-week course of cimetidine at 1,200 mg per day and diltiazem 60 mg per day. Ranitidine produced smaller, nonsignificant increases. The effect may be mediated by cimetidine's known inhibition of hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of diltiazem. Patients currently receiving diltiazem therapy should be carefully monitored for a change in pharmacological effect when initiating and discontinuing therapy with cimetidine. An adjustment in the diltiazem dose may be warranted.*

Digitalis: *Administration of CARDIZEM with digoxin in 24 healthy male subjects increased plasma digoxin concentrations approximately 20%. Another investigator found no increase in digoxin levels in 12 patients with coronary artery disease. Since there have been conflicting results regarding the effect of digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing CARDIZEM therapy to avoid possible over- or under-digitalization. (See WARNINGS.)*

Anesthetics: *The depression of cardiac contractility, conductivity, and automaticity as well as the vascular dilation associated with anesthetics may be potentiated by calcium channel blockers. When used concomitantly, anesthetics and calcium blockers should be titrated carefully.*

Carcinogenesis, Mutagenesis, Impairment of Fertility. *A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.*

Pregnancy. *Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.*

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. *Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.*

Pediatric Use. *Safety and effectiveness in children have not been established.*

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

Rx

Cardizem® (diltiazem HCl)

☐ 60 mg ☐ 90 mg
☐ 120 mg

Sig: tid

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	*Angina, arrhythmia, AV block (first degree), AV block (second or third degree—see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope.*
Nervous System:	*Amnesia, depression, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.*
Gastrointestinal:	*Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase.*
Dermatologic:	*Petechiae, pruritus, photosensitivity, urticaria.*
Other:	*Amblyopia, CPK elevation, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties.*

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

Issued 3/1/88

See complete Professional Use Information before prescribing.

References: ***1.*** *Schroeder JS: Mod Med 1982;50(Sept):94-116.* ***2.*** *Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39.* ***3.*** *O'Rourke RA: Am J Cardiol 1985;56:34H-40H.* ***4.*** *McCall D, Walsh RA, Frohlich ED, et al: Curr Probl Cardiol 1985;10(8):6-80.* ***5.*** *Frishman WH, Charlap S, Goldberger J, et al: Am J Cardiol 1985;56:41H-46H.* ***6.*** *Shapiro W: Consultant 1984;24(Dec):150-159.* ***7.*** *O'Hara MJ, Khurmi NS, Bowles MJ, et al: Am J Cardiol 1984;54:477-481.* ***8.*** *Strauss WE, McIntyre KM, Parisi AF, et al: Am J Cardiol 1982; 49:560-566.* ***9.*** *Feldman RL, Pepine CJ, Whittle J, et al: Am J Cardiol 1982;49:554-559.*

Another patient benefit product from

PHARMACEUTICAL DIVISION
MARION LABORATORIES, INC.
KANSAS CITY, MO 64137

1419H8

In Hypertension
Everything you want

VASO

(Enalapril Malea e-Hy

This fixed-dose combination is not indicated for initial therapy. Patients already receiving a diuretic when enalapril is initiated or given a diuretic and enalapril simultaneously can develop symptomatic hypotension. In the initial titration of the individual entities, it is important, if possible, to stop the diuretic for several days before starting enalapril or, if this is not possible, to begin enalapril at a low initial dose (2.5 mg; see DOSAGE AND ADMINISTRATION). This fixed-dose combination is not suitable for titration but may be substituted for the individual components if the titrated doses are the same as those in the combination.

VASERETIC, containing 10 mg enalapril maleate and 25 mg hydrochlorothiazide, is contraindicated in patients who are hypersensitive to any component of this product and in patients with a history of angioedema related to previous treatment with an ACE inhibitor. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

Evaluation of the hypertensive patient should always include assessment of renal function.

For a Brief Summary of Prescribing Information, please see last page of this advertisement.

Now Available on Medi-Cal

3134P

eretic®

drochlorothiazide (MSD)

Tablets

Vaseretic

ONCE-A-DAY

ACE PLUS

INHIBITION

Once-A-Day Vaseretic®

(Enalapril Maleate-Hydrochlorothiazide|MSD)

This fixed-dose combination is not indicated for initial therapy. Patients already receiving a diuretic when enalapril is initiated or given a diuretic and enalapril simultaneously can develop symptomatic hypotension. In the initial titration of the individual entities, it is important, if possible, to stop the diuretic for several days before starting enalapril or, if this is not possible, to begin enalapril at a low initial dose (see DOSAGE AND ADMINISTRATION in complete Prescribing Information). This fixed-dose combination is not suitable for titration but may be substituted for the individual components if the titrated doses are the same as those in the combination.

CONTRAINDICATIONS: VASERETIC is contraindicated in patients who are hypersensitive to any component of this product and in patients with a history of angioedema related to previous treatment with an ACE inhibitor. Because of the hydrochlorothiazide (HCTZ) component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

WARNINGS: ***Hypotension:*** Excessive hypotension was rarely seen in uncomplicated hypertensive patients but is a possible consequence of enalapril use in severely salt/volume-depleted persons, such as those treated vigorously with diuretics or patients on dialysis. Syncope has been reported in 1.3% of patients receiving VASERETIC and in 0.5% of patients receiving enalapril alone. The overall incidence of syncope may be reduced by proper titration of the individual components (see PRECAUTIONS, *Drug Interactions*; ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION in complete Prescribing Information). In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed and may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death. Because of the potential fall in blood pressure in these patients, therapy should be started under very close medical supervision. Such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased. Similar considerations may apply to patients with ischemic heart or cerebrovascular disease, in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident.

If hypotension occurs, the patient should be placed in a supine position and, if necessary, should receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses which usually can be given without difficulty once the blood pressure has increased after volume expansion.

Angioedema: Angioedema of the face, extremities, lips, tongue, glottis, and/or larynx has been reported in patients treated with ACE inhibitors, including enalapril. In such cases, VASERETIC should be promptly discontinued and the patient should be carefully observed until the swelling disappears. In instances where swelling has been confined to the face and lips, the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. **Where there is involvement of the tongue, glottis, or larynx likely to cause airway obstruction, appropriate therapy, e.g., subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL), should be promptly administered** (see ADVERSE REACTIONS)

Neutropenia/Agranulocytosis: Another ACE inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment, especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Foreign marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Hydrochlorothiazide: Thiazides should be used with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease since minor alterations of fluid and electrolyte balance may precipitate hepatic coma. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported. Lithium generally should not be given with thiazides (see PRECAUTIONS, *Drug Interactions: Hydrochlorothiazide*).

PRECAUTIONS: General: ***Enalapril Maleate:*** *Impaired Renal Function:* As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe congestive heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with ACE inhibitors, including enalapril, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in BUN and serum creatinine were observed in 20% of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients, renal function should be monitored during the first few weeks of therapy. Some patients with hypertension or heart failure with no apparent preexisting renal vascular disease have developed increases in BUN and serum creatinine, usually minor and transient, especially when enalapril has been given concomitantly with a diuretic. This is more likely to occur in patients with preexisting renal impairment. Dosage reduction of enalapril and/or discontinuation of the diuretic may be required. **Evaluation of the hypertensive patient should always include assessment of renal function.**

Hyperkalemia: Elevated serum potassium (>5.7 mEq/L) was observed in approximately 1% of hypertensive patients treated with enalapril alone in clinical trials. In most cases these were isolated values which resolved despite continued therapy, although hyperkalemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. Hyperkalemia was less frequent (approximately 0.1%) in patients treated with enalapril plus HCTZ. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements, and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with enalapril (see *Drug Interactions*).

Surgery/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving thiazide therapy should be observed for clinical signs of fluid or electrolyte imbalance: hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Warning signs or symptoms of fluid and electrolyte imbalance, irrespective of cause, include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.

Hypokalemia may develop, especially with brisk diuresis, when severe cirrhosis is present or after prolonged therapy. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Hypokalemia may cause cardiac arrhythmia and may also sensitize or exaggerate the response of the heart to the toxic effects of digitalis (e.g., increased ventricular irritability). Because enalapril reduces the production of aldosterone, concomitant therapy with enalapril attenuates the diuretic-induced potassium loss (see *Drug Interactions: Agents Increasing Serum Potassium*).

Although any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease), chloride replacement may be required in the treatment of metabolic alkalosis. Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice. Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy. In diabetic patients, dosage adjustments of insulin or oral hypoglycemic agents may be required. Hyperglycemia may occur with thiazide diuretics. Thus, latent diabetes mellitus may become manifest during thiazide therapy. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. If progressive renal impairment becomes evident, consider withholding or discontinuing diuretic therapy. Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia. Thiazides may decrease urinary calcium excretion. Thiazides may cause intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function. Increases in cholesterol and triglyceride levels may be associated with thiazide diuretic therapy.

Information for Patients: *Angioedema:* Angioedema, including laryngeal edema, may occur, especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue and/or difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness, especially during the first few days of therapy. If actual syncope occurs, patients should be told to discontinue the drug until they have consulted with the prescribing physician. All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion, such as vomiting or diarrhea, may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Hyperkalemia: Patients should be told not to use salt substitutes containing potassium without consulting their physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

NOTE: As with many other drugs, certain advice to patients being treated with VASERETIC is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions: ***Enalapril Maleate:*** *Hypotension—Patients on Diuretic Therapy:* Patients on diuretics, and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to enalapril treatment. If it is necessary to continue the diuretic, provide medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour (see WARNINGS and DOSAGE AND ADMINISTRATION). *Agents Causing Renin Release:* The antihypertensive effect of enalapril is augmented by antihypertensive agents that cause renin release (e.g., diuretics). *Other Cardiovascular Agents:* Enalapril has been used concomitantly with beta-adrenergic-blocking agents, methyldopa, nitrates, calcium-blocking agents, hydralazine, and prazosin without evidence of clinically significant adverse interactions. *Agents Increasing Serum Potassium:* Enalapril attenuates diuretic-induced potassium loss. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia, they should be used with caution and with frequent monitoring of serum potassium. *Lithium:* See WARNINGS, *Hydrochlorothiazide*; and PRECAUTIONS, *Drug Interactions: Hydrochlorothiazide*.

Hydrochlorothiazide: When administered concurrently, the following drugs may interact with thiazide diuretics: *Alcohol, barbiturates, or narcotics*—potentiation of orthostatic hypotension may occur. *Antidiabetic drugs (oral agents and insulin)*—dosage adjustment of the antidiabetic drug may be required. *Other antihypertensive drugs*—additive effect or potentiation. *Corticosteroids, ACTH*—intensified electrolyte depletion, particularly hypokalemia. *Pressor amines (e.g., norepinephrine)*—possible decreased response to pressor amines but not sufficient to preclude their use. *Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine)*—possible increased responsiveness to the muscle relaxant. *Lithium*—should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with VASERETIC. *Nonsteroidal anti-inflammatory drugs*—In some patients, the administration of a nonsteroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing, and thiazide diuretics. Therefore, when VASERETIC and nonsteroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

Pregnancy: ***Enalapril Maleate-Hydrochlorothiazide:*** *Pregnancy Category C.* There was no teratogenicity in rats given up to 90 mg/kg/day of enalapril (150 times the maximum human dose) in combination with 10 mg/kg/day of HCTZ (2-1/2 times the maximum human dose) or in mice given up to 30 mg/kg/day of enalapril (50 times the maximum human dose) in combination with 10 mg/kg/day of HCTZ (2-1/2 times the maximum human dose). At these doses, fetotoxicity expressed as a decrease in average fetal weight occurred in both species. No fetotoxicity occurred at lower doses: 30/10 mg/kg/day of enalapril-HCTZ in rats and 10/10 mg/kg/day of enalapril-HCTZ in mice.

There are no adequate and well-controlled studies of VASERETIC in pregnant women. VASERETIC should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Enalapril Maleate: Post-marketing experience with all ACE inhibitors thus far suggests the following with regard to pregnancy outcome. Inadvertent exposure limited to the first trimester of pregnancy has not been reported to affect fetal outcome adversely. Fetal exposure during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality.

When ACE inhibitors are used during the later stages of pregnancy, there have been reports of hypotension and decreased renal perfusion in the newborn. Oligohydramnios in the mother has also been reported, presumably representing decreased renal function in the fetus. Infants exposed *in utero* to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion with the administration of fluids and pressors as appropriate. Problems associated with prematurity, such as patent ductus arteriosus, have occurred in association with maternal use of ACE inhibitors, but it is not clear whether they are related to ACE inhibition, maternal hypertension, or the underlying prematurity.

Hydrochlorothiazide: Thiazides cross the placental barrier and appear in cord blood. *Nonteratogenic Effects:* These may include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

Nursing Mothers: It is not known whether enalapril is secreted in human milk; however, thiazides do appear in human milk. Milk of lactating rats contains radioactivity following administration of ^{14}C enalapril maleate. Because of the potential for serious reactions from HCTZ in nursing infants, a decision should be made whether to discontinue nursing or to discontinue VASERETIC, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: VASERETIC has been evaluated for safety in more than 1,500 patients, including more than 300 patients treated for one year or more. In clinical trials with VASERETIC, no adverse experiences peculiar to this combination drug have been observed. Adverse experiences that have occurred have been limited to those that have been previously reported with enalapril or HCTZ.

The most frequent clinical adverse experiences in controlled trials were dizziness (8.6%), headache (5.5%), fatigue (3.9%), and cough (3.5%). Generally, adverse experiences were mild and transient in nature. Other adverse experiences occurring in ~2% of patients treated with VASERETIC in controlled clinical trials were muscle cramps (2.7%), nausea (2.5%), asthenia (2.4%), orthostatic effects (2.3%), impotence (2.2%), and diarrhea (2.1%).

Clinical adverse experiences occurring in 0.5% to 2.0% of patients in controlled trials included: *Body as a Whole:* Syncope, chest pain, abdominal pain. *Cardiovascular:* Orthostatic hypotension, palpitation, tachycardia. *Digestive:* Vomiting, dyspepsia, constipation, flatulence, dry mouth. *Nervous/Psychiatric:* Insomnia, nervousness, paresthesia, somnolence, vertigo. *Skin:* Pruritus, rash. *Other:* Dyspnea, gout, back pain, arthralgia, hyperhidrosis, decreased libido, tinnitus, urinary tract infection. *Angioedema:* Angioedema has been reported in patients receiving VASERETIC (0.6%). Angioedema associated with laryngeal edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis, and/or larynx occurs, treatment with VASERETIC should be discontinued and appropriate therapy should be instituted immediately (see WARNINGS). *Hypotension:* In clinical trials, adverse effects relating to hypotension occurred as follows: hypotension (0.9%), orthostatic hypotension (1.5%), other orthostatic effects (2.3%). In addition, syncope occurred in 1.3% of patients (see WARNINGS).

Clinical Laboratory Test Findings: *Serum Electrolytes:* See PRECAUTIONS. *Creatinine, BUN:* In controlled clinical trials, minor increases in BUN and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.6% of patients with essential hypertension treated with VASERETIC. More marked increases have been reported in other enalapril experience. Increases are more likely to occur in patients with renal artery stenosis (see PRECAUTIONS). *Serum Uric Acid, Glucose, Magnesium, and Calcium:* See PRECAUTIONS. *Hemoglobin and Hematocrit:* Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g% and 1.0 vol%, respectively) occur frequently in hypertensive patients treated with VASERETIC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia. *Other (Causal Relationship Unknown):* Rarely, elevations of liver enzymes and/or serum bilirubin have occurred.

Other adverse reactions that have been reported with the individual components are listed below and, within each category, are in order of decreasing severity. *Enalapril Maleate*—Enalapril has been evaluated for safety in more than 10,000 patients. In clinical trials, adverse reactions which occurred with enalapril were also seen with VASERETIC. However, since enalapril has been marketed, the following adverse reactions have been reported: *Cardiovascular:* Cardiac arrest; myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients (see WARNINGS, *Hypotension*); pulmonary embolism and infarction; rhythm disturbances, atrial fibrillation; hypotension; angina pectoris. *Digestive:* Ileus, pancreatitis, hepatitis or cholestatic jaundice, melena, anorexia, glossitis. *Hematologic:* Rare cases of neutropenia, thrombocytopenia, and bone marrow depression have been reported in which a causal relationship to enalapril cannot be excluded. *Nervous System/Psychiatric:* Depression, confusion, ataxia. *Renal:* Renal failure, oliguria, renal dysfunction (see PRECAUTIONS and DOSAGE AND ADMINISTRATION). *Respiratory:* Bronchospasm, pneumonia, bronchitis, rhinorrhea, asthma, upper respiratory infection. *Skin:* Herpes zoster, alopecia, flushing, photosensitivity. *Other:* Vasculitis, blurred vision, taste alteration. A symptom complex has been reported which may include fever, myalgia, and arthralgia; an elevated erythrocyte sedimentation rate may be present. Rash or other dermatologic manifestations may occur. These symptoms have disappeared after discontinuation of therapy. *Hydrochlorothiazide—Body as a Whole:* Weakness. *Digestive:* Pancreatitis, jaundice (intrahepatic cholestatic jaundice), sialadenitis, cramping, gastric irritation, anorexia. *Hematologic:* Aplastic anemia, agranulocytosis, leukopenia, hemolytic anemia, thrombocytopenia. *Hypersensitivity:* Purpura, photosensitivity, urticaria, necrotizing angiitis (vasculitis and cutaneous vasculitis), fever, respiratory distress including pneumonitis and pulmonary edema, anaphylactic reactions. *Musculoskeletal:* Muscle spasm. *Nervous System/Psychiatric:* Restlessness. *Renal:* Renal failure, renal dysfunction, interstitial nephritis (see WARNINGS). *Special Senses:* Transient blurred vision, xanthopsia.

HOW SUPPLIED: No. 3418—Tablets VASERETIC 10-25 are rust, squared capsule-shaped, compressed tablets, coded MSD 720 on one side and VASERETIC on the other. Each tablet contains 10 mg enalapril maleate and 25 mg hydrochlorothiazide. They are supplied as follows: NDC 0006-0720-68 bottles of 100 (with desiccant).

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Summary.
Consult the package literature for prescribing information.

Indication: Lower respiratory infections, including pneumonia, caused by *Streptococcus pneumoniae, Haemophilus influenzae,* and *Streptococcus pyogenes* (group A β-hemolytic streptococci)
Contraindication: Known allergy to cephalosporins
Warnings: CECLOR SHOULD BE ADMINISTERED CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. PENICILLINS AND CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY. POSSIBLE REACTIONS INCLUDE ANAPHYLAXIS.

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:
- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- Ceclor should be administered with caution in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:
- Gastrointestinal (mostly diarrhea), 2.5%
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, and serum-sickness-like reactions that have included erythema multiforme [rarely, Stevens-Johnson syndrome]; and toxic epidermal necrolysis or the above skin manifestations accompanied by arthritis/arthralgia, and frequently, fever) 1.5%, usually subside within a few days after cessation of therapy. Serum-sickness-like reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.
- Other: eosinophilia 2%, genital pruritus or vaginitis, less than 1%, and, rarely, thrombocytopenia.

Abnormal values in laboratory results of uncertain etiology:
- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children).
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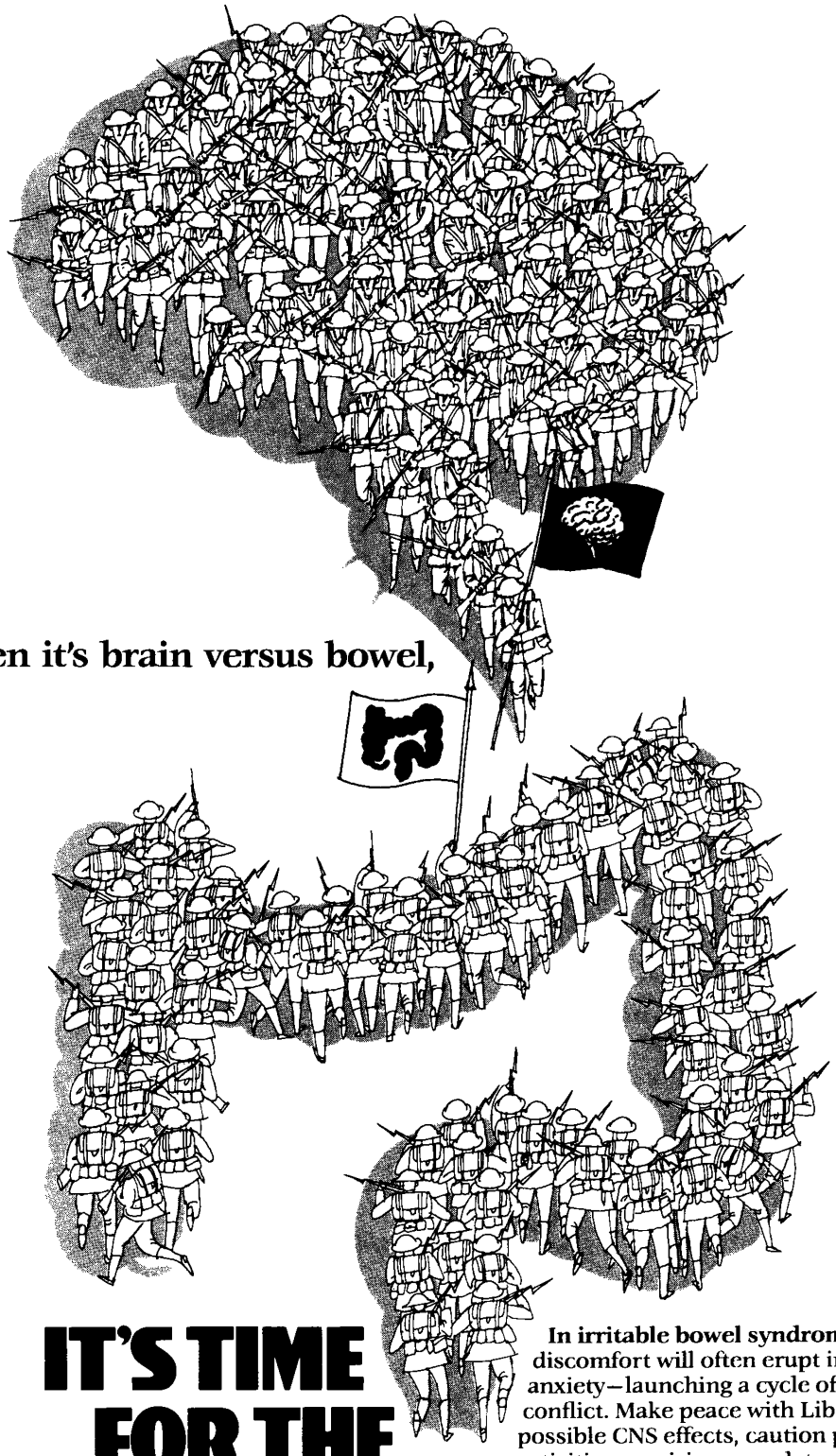

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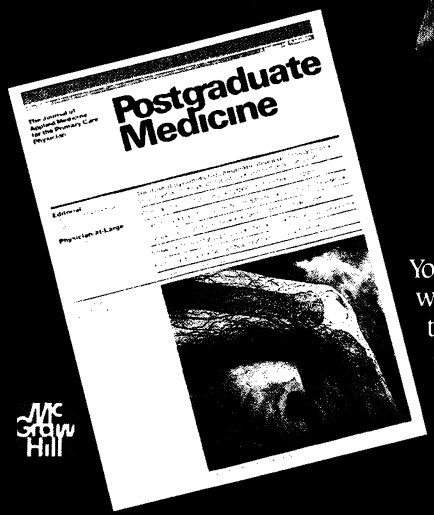

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For respiratory tract infections due to susceptible strains of indicated organisms.

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- Slight elevations in hepatic enzymes.
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- Abnormal urinalysis, elevations in BUN or serum creatinine.
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(Continued on Page 358)

(Continued from Page 356)

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521 Wall St
Seattle, WA 98121

SAN FRANCISCO BAY AREA. Full-time career Emergency Physician wanted for a high volume Emergency Department, 30 minutes south of San Francisco. Emergency Medicine BC/BE mandatory; prefer experienced. Congenial, democratic group of 20 full-time physicians doing some follow-up and minimal overnights. Competitive salary with excellent benefits including three to five weeks paid vacation; seven paid holidays; malpractice, medical, dental, and disability insurance; corporate shareholder in three years. Send CV or contact Drew Baker, MD, Kaiser Permanente Medical Center, 27400 Hesperian Blvd, Hayward, CA 94545; (415) 784-4521.

BC/BE FAMILY PRACTICE opportunity in Tucumcari, New Mexico. Must be willing to do OB. Financial assistance with income guarantee. For more information, please send CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

LOOKING FOR INTERNIST/FAMILY PRACTITIONER to join five physician group in Truckee, California. Northern Sierras at elevation 6,000 feet. Abundant recreation summer and winter—beautiful Lake Tahoe, restaurants, and skiing. 40-bed hospital with six ICU beds. Contact R. B. Ganong, MD, PO Box 2649, Olympic Valley, CA 95730; (916) 583-5320.

PSYCHIATRIST

BC/BE, part-time, possibly developing to full-time. Expanding San Francisco bay area practice emphasizing Occupational Medicine and med-legal evaluation seeks consulting Psychiatrist. Outstanding reputation, facilities and support staff, established referral base. Unique income opportunity. Submit CV and letter stating professional goals and availability to:

Personnel
Box 337
San Francisco, CA 94109

UNIVERSITY OF CALIFORNIA, DAVIS, MEDICAL CENTER. The University of California, Davis, Department of Emergency Medicine is in the second phase of an ambitious development plan and is searching for physicians residency trained in Emergency Medicine. The Health Sciences campus is located in Sacramento and serves a large area of northern California. The Emergency Department cares for over 60,000 patients a year. The Center operates as a Level I trauma center, has paramedic base station training responsibilities, and has a helicopter service. Emergency Physicians supervise medical students, interns, and residents in addition to having direct patient responsibilities. Support for clinical research is available to those interested. University compensation is competitive and fringe benefits include health and dental insurance, three weeks paid vacation, one week continuing medical education, social security, UC retirement plan, 12 paid holidays per year, and full malpractice coverage. Send CV to Robert W. Derlet, MD, Chief, Division of Emergency Medicine, University of California, Davis, Medical Center, 2315 Stockton Blvd, Sacramento, CA 95817.

SOUTHERN CALIFORNIA

Dynamic, multispecialty group is seeking Specialists and Primary Care Physicians for our facilities in Los Angeles and Orange Counties. Excellent compensation and benefit package. Please send CV to:

Robert Harrington, MD
CIGNA Healthplans of CA
505 N. Brand Blvd, #400-49
Glendale, CA 91203
or call collect (818) 500-6570

(Continued on Page 359)

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PHYSICIANS WANTED

BC/BE INTERNIST being recruited for the community of Artesia, New Mexico. Solo practice with cross-coverage available from local Internist. Community-based financial assistance may be available for the right individual. Family oriented community with year round recreation; excellent weather. Fully equipped 38-bed hospital. For more information, please send CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

BC/BE FAMILY PRACTITIONER sought to join an established practice in the community of Artesia, New Mexico. Income guarantee available for the right individual. Family oriented community with year round recreation and fully equipped 38-bed hospital. Please send CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

CALIFORNIA, NORTHERN. A stable group of four ABEM certified/eligible MDs at coastal hospital of 24,000 patient visits would like two new associates. Income $60-$75 per hour. Will consider Family Practice but prefer Emergency Department trained Emergency Physician. Coastal paradise near redwood national parks, minutes from Klammath, Rouge, and Smith Rivers. Video tape of area available. Send CV to EPMG, 120 Montgomery St, Ste 1825, San Francisco, CA 94104.

RADIOLOGIST. Part-time position available immediately in small hospital with general radiography and fluoroscopy, mammography and ultrasound in Weaverville, California. Contact Drs Wheeler, Biggs, or Babbitt, West Coast Radiology, 3798 Janes Rd, Ste 12, Arcata, CA 95521; office number (707) 822-3621, ext 191.

PATHOLOGIST. AP-CP to join three BC AP-CP with special competence, certified in Dermatopathology, Immunohematology, and Immunopathology. 300-bed progressive acute care hospital. Adding a fourth Pathologist due to workload. Must have or be willing to develop a forté in Microbiology in addition to sharing AP workload. State-of-the-art medicine. All medical and surgical subspecialties represented. Boise, Idaho's capital city, has an enviable four season climate with abundant recreational outlets. World class fine arts center. Four year college with large stadium and sports pavilion. Downtown parks and river known for float trips and fishing. Six double chair lift skiing 16 miles away. Excellent schools. Great place to raise a family. Competitive income. Desire recently trained individual. All details first letter. No phone calls please. Reply to John C. Day, MD, 190 E. Bannock, Boise, ID 83712.

INTERNAL MEDICINE. Long established multispecialty group in central Washington needs Internist. Independent contract or join partnership later. University town with many cultural and recreational activities. Send CV to Medical Building Associates, 200 E. 6th, Ellensburg, WA 98926, or call (509) 925-9891.

SACRAMENTO AMBULATORY/URGENT CARE. Part-time openings for Family Practitioners and Internists with experience in adult ambulatory care. Clinic operates 12 hours per day, seven days a week for acute care. Flexible scheduling. Benefits available for physicians working at least six half days per week on a regular basis. Contact Stuart Hahn, MD, (916) 973-5546, or request application from Carolyn Whelan, Physician Recruiting, The Permanente Medical Group, Inc, 2025 Morse Ave, Sacramento, CA 95825. EOE.

FAMILY PRACTICE, NORTHERN CALIFORNIA. Immediate opening. Competitive salary. Excellent benefits. Malpractice provided. Contact Debra Pahl, CTHP, 564 S. Dora St, Ste D, Ukiah, CA 95482; (707) 468-5341.

(Continued on Page 360)

NORTHERN CALIFORNIA

The Permanente Medical Group, a growing multispecialty group, is recruiting physicians in a variety of specialties for positions throughout our beautiful Northern California region: the San Francisco Bay Area, Sacramento and the Central Valley.

MARTINEZ

Emergency Physicians — Join friendly, relaxed and highly professional colleagues at our 204-bed hospital in the heart of the San Francisco Bay Area. We are seeking experienced physicians, BE/BC preferred. Locum Tenens and part-time work available Summer/Fall, 1989 & Winter/Spring, 1990. Recent adjustments provide excellent hourly rate plus paid malpractice. Career positions also available, providing salary and excellent benefits package. Send CV to: Ted Bayer, M.D., Chief, or Andrea Wagner, M.D., Asst. Chief, Department of Emergency Services, The Permanente Medical Group, Inc., 200 Muir Road, Martinez, CA 94553. (415) 372-1000, ext. 3316 or (415) 372-1124.

Internists and Cardiologist (BC/BE) - Join us in our high quality, expanding, 25 member Department of Medicine where you will benefit from our university affiliated internal medicine residency program. Faculty appointment available. This East Bay suburban setting has excellent schools, and is only 25 miles from San Francisco. Please send CV, or contact Michael Melewicz, M.D., Dept. of Medicine, The Permanente Medical Group, Inc., 200 Muir Road, Martinez, CA 94553. (415) 372-1069.

ROSEVILLE

General Internists (BC/BE) — Immediate openings for California licensed Internists at our Roseville facility, 90 miles from San Francisco or Sierra skiing & camping. University associated residency program. Send CV to: Tony Cantelmi, M.D., The Permanente Medical Group, Inc., 1001 Riverside Blvd., Roseville, CA 95678.

SAN JOSE

Family Practitioner (BC/BE) — Our 228-bed Santa Teresa Medical Center serves 128,000 members. Predominately outpatient practice located in Silicon Valley, approximately 45 minutes south of San Francisco and 30 minutes from the Pacific Coast. Send CV to D. Bardole, The Permanente Medical Group, Inc., 260 International Circle, San Jose, CA 95119.

Surgeons (BC/BE) - One General Surgeon and one Surgeon to do both general and vascular surgery. We are a 9 surgeon department with modern offices adjacent to the 228-bed hospital equipped with 7 operating rooms. We handle a full range of general, thoracic, vascular and plastic surgery cases, and our group includes about 100 fully trained physicians in all specialties. Please apply to the Oakland address below.

SOUTH SAN FRANCISCO

Seeking highly-motivated **BC/BE Internists and a BC/BE Gastroenterologist-Internist** for this expanding practice adjacent to our 125-bed community hospital. Send CV to: Mark Cole, M.D., Dept. of Medicine, The Permanente Medical Group, Inc., 1200 El Camino Real, So. San Francisco, CA 94080.

FAIRFIELD

Excellent opportunity for **BC/BE Family Practitioner** to join a growing department. Multispecialty clinic emphasizing personalized care. Full hospital privileges including ICU/CCU, but no Obstetrics. Very favorable call schedule. Forward CV to: Steven Freedman, M.D., The Permanente Medical Group, Inc., 1550 Gateway Blvd., Fairfield, CA 94533. (707) 427-4260.

Members of our large, multispecialty group earn a highly competitive salary and excellent benefits including scheduled time off, malpractice insurance, medical, dental and life insurance, and a substantial retirement program. Our physicians are free to concentrate on providing quality health care, without the burdens of managing a practice.

To inquire about other openings with our successful, growing medical group, send CV to: Richmond Prescott, M.D., Physician Recruitment Services, Dept. WJM-5114, The Permanente Medical Group, Inc., 1814 Franklin, 4th Floor, Oakland, CA 94612. (415) 987-4949. EOE

KAISER PERMANENTE

Good People. Good Medicine.

(Continued from Page 359)

PHYSICIANS WANTED

NORTH CENTRAL IDAHO

17 physician multispecialty group recruiting BC/BE partners.

- 2nd Dermatologist
- 2nd Gastroenterologist
- 3rd General Internist
- 6th Pediatrician

Progressive medical community. Outstanding recreational area. Excellent life-style.

Send CV to:

Bob Baker, Administrator
Valley Medical Center and Children's Clinic
2318 Vineyard Ave
Lewiston, ID 83501
(208) 746-1383

SAN FRANCISCO MEDICAL DIRECTOR AND PHYSICIANS

For establishing community clinic with ethnically diverse patients, 21,000 patient visits per year. BC/BE Family Physician for above positions. Full-time/part-time, available now. Medical directorship would include 50 percent administrative time for assistance with grants, quality assurance, etc. Academic appointment, prenatal care, and teaching opportunities. Excellent benefits, competitive salary. MPH and administrative experience preferred for Medical Director.

Send CV to: **Michael Williams, SFMCOIP, Inc, PO Box 40519, San Francisco, CA 94140.**

SAN FRANCISCO BAY AREA. BE/BC Internist. We currently are seeking highly qualified Internists and subspecialists to complement our energetic Internal Medicine team. Department members provide a full range of medical services for a population of over 200,000 prepaid Health Plan members. Recently renovated and expanded medical center facilities are within convenient commuting distance to virtually any bay area city and the extensive cultural and recreational activities of northern California. As part of our large, multispecialty group practice, you would enjoy an excellent salary, generous fringe benefits, a flexible schedule, and the opportunity for academic affiliation with prestigious local institutions. Send CV to Michael Getzell, MD, Chief, Dept of Internal Medicine, Kaiser Permanente Medical Center, 27400 Hesperian Blvd, Hayward, CA 94545.

SAN FRANCISCO. Seeking BE/BC Internist for part-time or full-time locum tenens in busy department of medicine with full subspecialty backup. Excellent salary and full benefits if working six or more half days. California license essential. Contact Paul Feigenbaum, MD, Chief of Service, Kaiser Permanente, 2200 O'Farrell St, San Francisco, CA 94115; (415) 929-2665. EOE.

GENERAL PRACTICE—SOUTHEAST WASHINGTON. 32 physician multispecialty clinic needs full-time physician as second physician in Immediate Care Center. Center is part of main clinic and has full range of ancillary and consultative services available. Abundant free time with no on-call responsibility. Excellent school system. Outstanding recreational and cultural opportunities. Guaranteed salary with excellent fringe benefits. Contact Robert Caudill, MD, or David Maloney, Administrator, Walla Walla Clinic, 55 W. Tietan, Walla Walla, WA 99362; (509) 525-3720.

INTERNIST. BC/BE Internist wanted to join Internal Medicine group practice. Competitive salary and excellent fringe benefits. Early partnership. Send CV to Number 162, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602, or call Sara Brenner, (213) 478-5913.

PHYSICIANS WANTED

OCCUPATIONAL HEALTH MEDICINE

OGDEN, UTAH

McKay-Dee Hospital Center, located 30 miles north of Salt Lake City, is seeking a Physician to provide medical treatment for injury/illness care, and perform physical examinations in our Ogden and Salt Lake City WorkMed Clinics. Will also assist in policy and procedure development, training medical staff, and participate in sales/marketing meetings and activities as required. Assists in QA development and analysis. Internal medicine or emergency room training/experience helpful. Must be licensed physician or licensure eligible and be a graduate of an approved/accredited school of medicine. Excellent benefits and competitive salary enhance this position. Enjoy the Utah adventure...

Submit CV to : **JoLynn Richards, Human Resources Department, 3939 Harrison Boulevard, Ogden, Utah 84409. 1-801-625-2061.**

McKAY-DEE HOSPITAL CENTER

A Facility of Intermountain Health Care
An Equal Opportunity Employer M/F/H/V.

DIAGNOSTIC RADIOLOGIST to associate with six physician group at county hospital (major trauma center) and private office partnership after two years. Start early September or by arrangement. Equal Opportunity Employer. Contact L. Preger, MD, (415) 437-4205, Highland Hospital, 1411 E. 31st St, Oakland, CA 94602.

BC/BE INTERNIST being sought to establish practice in resort community of Ruidoso, New Mexico. Beautiful mountain setting with easy access to all forms of recreation. Financial assistance may be available for the right individual. For more details, please send CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext 8300.

GYNECOLOGIST needed for 78-bed JCAHO hospital. We are growing and we need to enlarge our specialty staff. Just opened new Cancer Treatment Center. 12,000 community, 90,000 immediate service area, 160,000 catchment area. Great outdoors area, cattle, oil, gas, hunting, fishing, good schools, low crime, ideal area for raising children. Reasonable malpractice rates. Send CV to Marilyn Bryan, Community Hospital, PO Box 2339, Elk City, OK 73648; (405) 225-2511.

INTERNAL MEDICINE, SEATTLE. BE/BC full-time Primary Care, to join two other Internists now. Well established growing progressive practice near major north end hospital. Income guarantee first two years. CV to Internal Medicine, 540-C NE Northgate Way, Ste 139, Seattle, WA 98125.

SAN FRANCISCO AREA. Family Practitioner or Primary Care Internist to join progressive six physician group in lovely coastside community of Half Moon Bay, 25 miles south of San Francisco. CV to Dr Larry Casalino, 225 S. Cabrillo Hwy, Half Moon Bay, CA 94019.

GENERAL INTERNIST/NEUROMUSCULAR/COPD / REHABILITATION. We are seeking a BC/BE General Internist to join the staff of a 48-bed respiratory unit at an internationally recognized rehabilitation center affiliated with the University of Southern California. Must demonstrate interest in management of respiratory-neuromuscular/chest wall disorders, COPD and tuberculosis. Some critical care. Busy exercise lab. Opportunity in clinical investigation. Clinical faculty appointment at USC, depending on qualifications. Interested individuals should send CV to Ahmet Baydur, MD, Chest Medicine Service, Rancho Los Amigos Medical Center, 7601 E. Imperial Hwy, Downey, CA 90242. Equal Opportunity/Affirmative Action Employer.

GENERAL INTERNIST. Group practice located in beautiful northern California wine country seeks General Internist. We are opening a new 106-bed hospital February 1990; a superb opportunity to join a growing, thriving practice. Excellent salary, benefits, security, and ample time off. Please send CVs to Richard Zweig, MD, 401 Bicentennial Way, Santa Rosa, CA 95403-2192.

SOUTHERN CALIFORNIA

Exciting opportunity for Dermatologist to develop an interesting and challenging practice in sophisticated metropolitan Los Angeles area. Easy access to major academic centers, cultural and recreational activities. Superb salary and benefits. Send CV to:

Director/Professional Recruitment
CIGNA Healthplans of California
505 N. Brand Blvd, Ste 400-49
Glendale, CA 91203
or call collect (818) 500-6236

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PHYSICIANS WANTED

CALIFORNIA, WESTERN STATES, AND TEXAS
Opportunities for BE/BC physicians in ENT, Internal Medicine, Family, General Surgery, Pediatrics, OB/GYN, Orthopedics, Urgent Care, and others. Phone or send CV to **Bradshaw Associates, 21 Altamount, Orinda, CA 94563; (415) 376-0672 or FAX (415) 376-0813.**

FAMILY PRACTITIONERS AND GENERAL INTERNISTS, Sacramento Kaiser Permanente. Must be BC/BE. Family Practitioners join 23 Family Practitioners with excellent consultant support. Internists work in established Department of Medicine, experience continuing growth. Pleasant practice setting where physicians are free to provide the highest quality medicine with full access to diagnostic and therapeutic services. Affiliated with University of California, Davis, providing a substantial part of their residency programs. Excellent financial package includes in-house CME and retirement package, with no billing or practice management headaches. To join our successful, growing medical group, Family Practitioners send CV to Stuart Hahn, MD, The Permanente Medical Group, Inc, 3240 Arden Way, Sacramento, CA 95825. Internists send CV to Dennis Ostrem, MD, The Permanente Medical Group, Inc, 2025 Morse Ave, Sacramento, CA 95825; (916) 973-5781. EOE.

CALIFORNIA, SAN FRANCISCO BAY AREA. Saint Louise Health Center is a new hospital scheduled to start operations October 1. This is an exciting opportunity for BC/BE Emergency Physicians to organize and start-up a level II emergency service. Located in Morgan Hill, a high growth desirable residential area on the outer fringe of Silicon Valley, this position includes membership in a prestigious northern California staffing group which is democratically governed and academically oriented. Please mail CV to Kate Lawlor, Emergency Physicians' Medical Group, 120 Montgomery St, Ste 1000, San Francisco, CA 94104.

BEAUTIFUL MONTEREY BAY. Immediate opportunity for a friendly, skilled, Family Practice or Emergency Physician to join highly respected urgent care group with two beautiful Santa Cruz clinics. Committed to high quality care. Nice people, flexible scheduling, comprehensive benefits, including paid malpractice, group health insurance, long-term disability insurance, no nights, rapid advancement to full partnership in an outstanding place to live. Please send CV to Robert Korns, MD, 6800 Soquel Dr, Aptos, CA 95003 or call (408) 662-3611.

SAN FRANCISCO. Well established General Internist seeks BE/BC associate, private practice, some Geriatric emphasis, benefit package includes incentive options, pension funds, malpractice. Contact Martin Lorber, 1500 Southgate Ave, Daly City, CA 94015; (415) 992-4466.

EUGENE CLINIC, EUGENE, OREGON
Dynamic 55 physician multispecialty group with seven locations seeks BC/BE physicians in the following specialties: Dermatology, Family Practice, Geriatrics, Infectious Diseases, Internal Medicine, OB/GYN, Occupational Medicine, Orthopedics, General Surgery (breast disease focus), Urology. Eugene, attractive university town within 60 mile radius of Cascade Mountains and Oregon coast, offers superlative life-style, fine school system, active and varied cultural opportunities, and unlimited recreation. Qualified candidates send CV and three letters of reference to:

Physician Recruiter
1162 Willamette St
Eugene, OR 97401

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PHYSICIANS WANTED

PHYSICIANS NEEDED

The continuing growth of our service area population (now 90,000) has created an immediate need for additional BC/BE physicians in the following specialties:

- **OB/GYN.** Establish private practice with no investment. Guaranteed income. Hospital has newly designed Single Room Maternity Care and new Women's Health Center.
- **FAMILY PRACTICE.** Guaranteed income while you develop your own private practice. Share beautiful office with young, BC Family Practitioner in a flourishing practice (No OB). No investment required.
- **ONCOLOGY.** Establish private practice with no investment, guaranteed income. Some Internal Medicine necessary initially. 112-bed full service hospital with excellent ancillary services.
- **RADIOLOGY.** Hospital group position. Excellent salary and benefit package. Competency in ultrasound, CAT, Nuclear Medicine, film screen mammography, and general diagnosis required. MRI experience desired. Inpatient and outpatient.

Located in central California near Sequoia National Park, Tulare offers a family oriented environment, abundant and varied recreation, good schools, restaurants, and shopping. Beautiful, affordable homes close to hospital and office. Strong economy. New businesses are contributing to the steady growth of our active community which combines the life-style advantages of a small city with easy access to all California attractions.

Contact:

Tulare District Hospital
Physician Recruiting
Office, PO Box 90112,
Los Angeles, CA 90009;
(213) 216-2687.

PHYSICIANS WANTED

IMMEDIATE OPENINGS IN CALIFORNIA CENTRAL COAST GROUP PRACTICE

Growing multispecialty group practice
in Ventura, California
seeks Board Certified/Eligible:

- Orthopedic Surgeon
- Pediatrician
- Family Practitioners
- Cardiologist
- Pulmonologist
- Psychiatrist
- Internist

We offer competitive compensation and excellent benefits; shareholdership option after 1 year. Located 60 miles north of Los Angeles, our community is one of the most beautiful areas in California, with excellent schools, a strong economy, and a wide range of cultural and recreational activities. Call for more information. Send inquiries and Curriculum Vitae to:

A Tradition of Service Since 1950

Buenaventura Medical Clinic

2705 Loma Vista Road Ventura, California 93003 (805) 648-2571

PHYSICIANS
Immediate Opportunities!
SAN DIEGO

JSA, Inc., is currently offering physicians full, part-time, and PRN positions in a Primary Care Clinic located in San Diego, a JCAHO accredited facility.

BENEFITS PACKAGE

- **Flexible day-time hours**
- **No "on-call" requirement**
- **Paid malpractice insurance**
- **Professional development funding**
- **Incentive programs**
- **Exceptional salary level**

QUALIFICATIONS

- **BE or BC in Family Practice, Emergency Room, or Internal Medicine**
- **MD or DO**
- **Current state licensure**
- **ACLS/BCLS**

Please contact Susan Bray, Recruiting Director at (301) 964-2811, or the Clinic Medical Director at (619) 424-3403.

JSA HEALTHCARE
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BC PHYSICIANS MANAGED CARE

Cost Care, the nation's leading health care cost management company, is seeking full- or part-time BC physicians to staff the Medical and Mental Health Services departments. Ideal candidates will have:

- Three to five years clinical experience in a managed care setting
- Utilization Review expertise
- Strong interpersonal skills

Send résumé/CV to:

Alan R. Greenfield, MD
VP Medical Services
Cost Care, Inc
17011 Beach Blvd, Ste 400
Huntington Beach, CA 92647

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Your reputation and your business are put on the line every day. It's the same at SCPIE.

Our reputation depends upon how well we serve our policyholder-owners. We perform accordingly.

That is why SCPIE is a national leader in its field.

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(619) 544-0163 (In San Diego)

Sponsored by the Medical Associations and Societies of Kern, Los Angeles, Orange, Riverside, San Luis Obispo, San Bernardino, Santa Barbara and Ventura Counties. Available elsewhere in California. Also sponsored by the California Association of Oral and Maxillofacial Surgeons.

(Continued from Page 362)

PHYSICIANS WANTED

KAISER PERMANENTE

Good People. Good Medicine.

NORTHERN CALIFORNIA

Several positions available for Family Practice, Internal Medicine, and most medical subspecialties. We are a young, aggressive group in a well known prepaid group practice HMO organization with excellent benefits and a very reasonable call schedule. You will have a rewarding practice opportunity with ample time to enjoy the mountains and San Francisco which are nearby. If interested please call or send CV to Physician Recruitment, Administration, The Permanente Medical Group, Inc, 1305 Tommydon St, Stockton, CA 95210; (209) 476-3300.

VP MEDICAL SERVICES for Medi-Cal prepaid health plan and fee-for-service community health center. Responsible for Quality Assurance, Utilization Review, provider staffing. Excellent salary and fringe benefits. California license, two years management experience in HMO setting, and formal management training. CV to President/CEO, PO Box 30051, San Jose, CA 95156-9985. EOE.

FAMILY PRACTICE, KENT, WASHINGTON. Established Family Practice clinic looking for full-time physician. Excellent salary. Production incentive available for practice builders. Partnership potential. Contact Lisa Barry at Covington Medical Clinic, 17128 SE 272nd, Kent, WA 98042; (206) 630-3100.

SEATTLE/TACOMA AREA. North Pierce/South King County area. Primary Care Physician needed for established practice. Financial assistance available. High growth area. Young families. For details, call Eloise Gusman, 1 (800) 535-7698 or (504) 893-4879 or send CV to PO Box 1685, Covington, LA 70433.

SAN DIEGO. Well established, multispecialty group composed of Family Physicians, General Internists, OB/GYNs, Pediatricians, General Surgeons, ENT, and Ophthalmologist is expanding. Those interested in joining a vital private practice group, with emphasis in primary care and seeing fee-for-service and managed care patients, are welcome to send CV to Miriam Stephens Drake, 1450 Frazee Rd, Ste 605-1, San Diego, CA 92018; (619) 295-0599.

ACADEMIC GENERAL INTERNIST. The University of Utah School of Medicine, Division of General Medicine is offering full-time positions for BE/BC Internists at the instructor/assistant professor/associate professor levels. Rank and salary commensurate with qualifications. Opportunities include patient care, teaching of medical students and residents, administration, and clinical research. Applications must be postmarked by October 30, 1989; applications submitted after the deadline may be considered if no qualified candidates have applied by that deadline. An Equal Opportunity Employer. Contact John H. Holbrook, MD, Dept of Internal Medicine, University Hospital 4B-120, Salt Lake City, UT 84132.

UROLOGIST, southern California. Urology group seeking new highly qualified BC partner. Ability in all radical surgery, ESWL, Endourology, prostheses, etc desired. Excellent smog-free coastal locale. Busy, expandable practice. Send CV to Number 157, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PHYSICIANS WANTED

FAMILY PRACTITIONER. Excellent opportunity in the culturally rich, 4-Corners area of northwest New Mexico. All aspects of Family Practice including prenatal. No deliveries. Outstanding benefit package. Recreational paradise in community of 30,000. Call or send CV to Sheila Brenner, Physician Recruiter, Farmington Community Health Center, PO Box 3239, Farmington, NM 87499; (505) 327-4796.

FAMILY PRACTITIONER. BC/BE to join eight member Family Practice department in multispecialty group. No OB. Near Sacramento. Send CV to Caroline Brown, MD, Dept of Family Practice, Woodland Clinic Medical Group, 1207 Fairchild Ct, Woodland, CA 95695.

CALIFORNIA. BC/BE HEMATOLOGIST/ONCOLOGIST to join 14 MD multispecialty group with progressive practice environment located in a small city in the central San Joaquin Valley at the foothills of the Sierras, two hours from the coast. Send CV to Kaweah Medical Group, Attn: Maya Ricci, 222 W. Willow, Visalia, CA 93291.

CALIFORNIA. BC/BE OTOLARYNGOLOGIST to join 14 MD multispecialty group with progressive practice environment located in a small city in the central San Joaquin Valley at the foothills of the Sierras, two hours from the coast. Send CV to Kaweah Medical Group, Attn: Maya Ricci, 222 W. Willow, Visalia, CA 93291.

MULTIPLE FAMILY PRACTICE (BC/BE) positions available in several suburban satellite clinics of a large Seattle area multispecialty group practice. Diverse patient population includes managed care, fee-for-service, and retired military (at some satellite clinics). Competitive salary and excellent benefits. Contact Mary Anderson, Pacific Medical Center, 1200 12th Ave S., Seattle, WA 98144; (206) 326-4111.

NAPA, CALIFORNIA. BC Internist. Location in Napa, heart of the wine country. Close to San Francisco. Offering either professional association or solo practice start-up. Includes attractive income guarantee. Send CV and two letters of recommendation (Department Chief if applicable) to Alvin L. Block, MD, 3230 Beard Rd, Napa, CA 94558; (707) 257-1550.

PHYSICIANS WANTED

PROGRESSIVE MULTISPECIALTY GROUP

of over 20 physicians, located in Tracy, one of the most rapidly growing cities in northern California. Located in the San Joaquin Valley with diversified economy and excellent schools. We are looking for the following:

DERMATOLOGY
OTOLARYNGOLOGY
OB/GYN
NEUROLOGY
ORTHOPEDICS
PEDIATRICS
PODIATRY

Applicants must be BC/BE. Offering an excellent salary with an incentive arrangement and a competitive benefit package, leading to partnership after 18 months.

Reply with CV and references to:

Physician Recruitment
Eaton Medical Group
445 W. Eaton Ave
Tracy, CA 95376

BC/BE FAMILY PRACTITIONER for diverse practice in rural Minnesota. Join busy group of three Family Practitioners and replace retiring senior member. Minor Obstetrics, one in three call. Excellent quality of life in beautiful lakeside location 45 minutes from St Cloud. Competitive financial package includes guarantee plus bonus, benefits, insurance, malpractice, relocation, and all expenses. Contact Paul Clukies, Jackson & Coker, 400 Perimeter Center Terrace, Ste 760 WJM9, Atlanta, GA 30346; 1 (800) 544-1987.

WASHINGTON STATE
ROCKWOOD CLINIC, PS

An expanding 65 physician multispecialty fee-for-service group seeks BC/BE physicians in the following specialties:

ALLERGY	HEMATOLOGY/ONCOLOGY
CARDIOLOGY	OB/GYN
DERMATOLOGY	RHEUMATOLOGY
INTERNAL MEDICINE	GENERAL SURGERY

FAMILY PRACTICE—permanent, part-time, locum tenens

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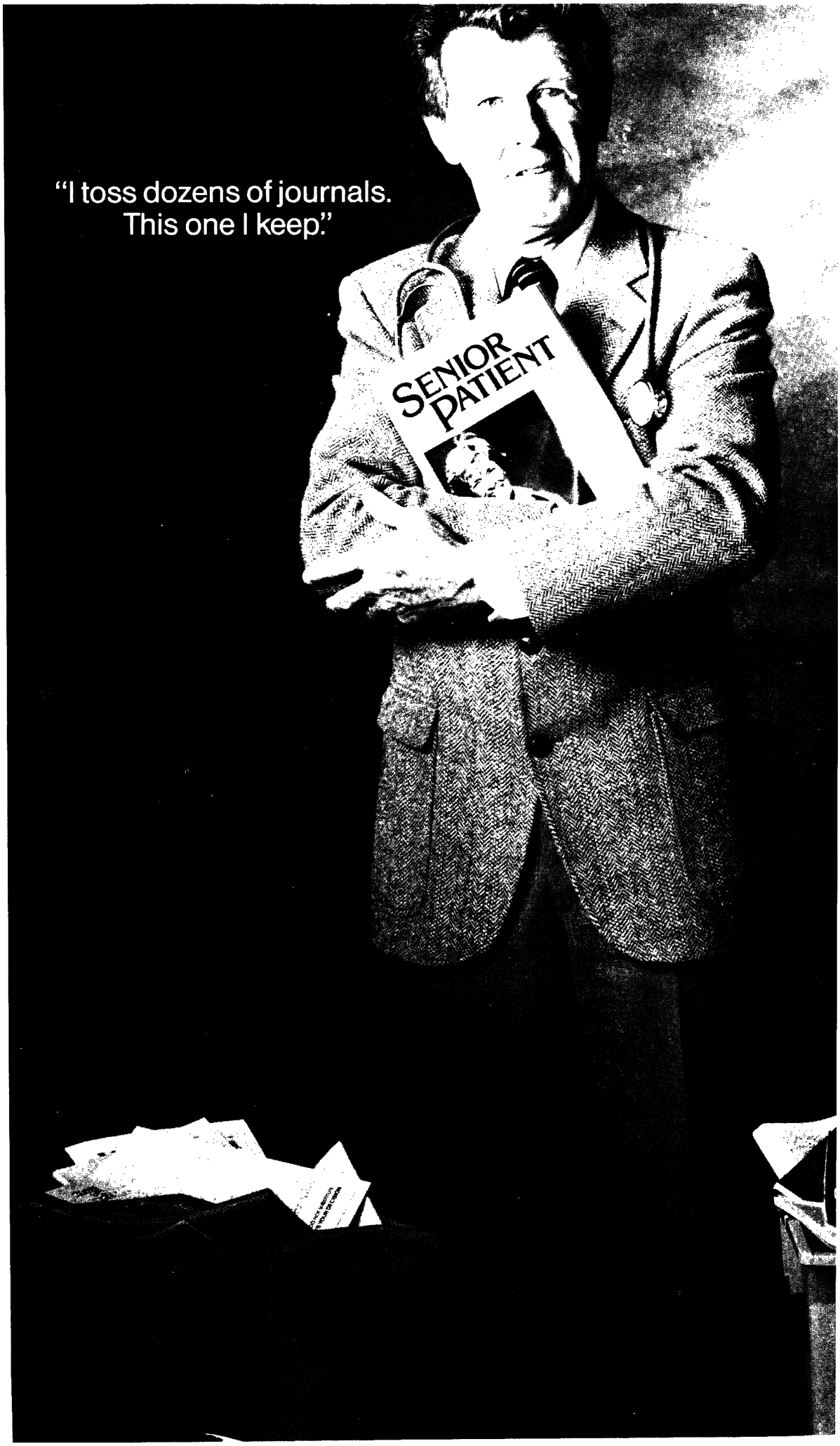

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(Continued from Page 364)

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SAN FRANCISCO. Outstanding opportunity for BC/BE Internist or Family Practitioner at 260-bed community hospital in the rapidly growing South of Market area. Excellent opportunity to build or join busy practices. Competitive salary and benefits package. Send CV to Walter Kopp, St Luke's Hospital, 3555 Army St, San Francisco, CA 94110; (415) 641-6543.

ONCOLOGIST NEEDED for multispecialty group practice in Seattle; affiliated with University of Washington. Full-time clinical with potential for research. Diverse patient population includes managed care, fee-for-service, retired and active duty military. Attractive salary plus incentive and excellent benefit package. Send CV or contact Mary Anderson, Personnel Representative, Pacific Medical Center, 1200 12th Ave S., Seattle, WA 98144; (206) 326-4111.

PHYSICIAN OPPORTUNITIES NATIONWIDE
For all specialties for hospitals, clinics, multispecialty groups, partnership and solos. Contact Jim Grant in complete confidence at the bay area specialists, **Len Nugent and Co, 1556 Halford Ave, Ste 181, Santa Clara, CA 95051; or call (408) 984-8293, FAX # (408) 984-0412.** Never a fee to the physician.

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CHIEF OF PROFESSIONAL CLINICAL SERVICES. Official County Title: Principal Public Health Physician. Challenging opportunity for experienced physician to plan and supervise professional services in all public health clinics in Riverside County, one of the fastest growing counties in California. Salary: $58,219-$72,134 and employer paid PERS. Excellent benefits. For detailed requirements and application materials contact Riverside County Personnel Dept, 4080 Lemon St, Room 109, Riverside, CA 92501-3664; (714) 787-6125. EOE AA M/F/H.

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INTERNIST. Live in San Francisco and commute to nearby rural area for four two-night shifts per month in combined Internal Medicine/Emergency Room practice. Five Internists currently working in stable group. Practice quality medicine in the country where you can make a greater impact and enjoy lots of free time wherever you like to live. $72k per year. Charles Rath, MD, 199 E. Webster St, Colusa, CA 95932; (916) 458-7739.

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SAN FRANCISCO BAY AREA—GENERAL INTERNIST. BC/BE General Internist needed immediately for half-time practice at the Palo Alto Medical Clinic. This is a job sharing situation with another General Internist. This is a multispecialty group affiliated with Stanford University Hospital. Please send CV to Deirdre Stegman, MD, Palo Alto Medical Clinic, 300 Homer Ave, Palo Alto, CA 94301.

PSYCHIATRIST. Full- or part-time position, innovative team working with senior citizens, med evaluations, consultations, some supervision. $300 to $600 per day. National Institute for Behavior Change, (303) 296-2244; ask for Lois Munson.

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GENERAL SURGEON—SAN FRANCISCO BAY AREA. Small group of well established, BC General Surgeons are now seeking to add another member with two to three years practice experience. Send CV to Manager, Professional Relations, PO Box 1438, Dept HH-9A, Louisville, KY 40201-1438; or call toll-free, 1 (800) 626-1590.

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TUCSON, ARIZONA. BC/BE, residency trained Family Physician sought to join busy solo Family Physician in private practice. Attractive start-up package available. Send CV to Herb Jalowsky, MD, 1701 W. St Mary's Rd, Tucson, AZ 85745; (602) 622-1414.

PEDIATRICIAN for State Health Division, Special Children's Clinic, Reno, Nevada. Must be BE/BC. Preference will be given to a candidate experienced in developmental pediatrics. Salary commensurate with credentials to a maximum of $80,029. Liberal benefits. Call (702) 786-0241 for further information.

CENTRAL CALIFORNIA. Join our team of Family Practice Physicians in a community health clinic setting near Fresno, California. We offer a contract arrangement with competitive salaries and benefits, malpractice paid. We are affiliated with the UC San Francisco teaching program. Central California has Yosemite National Park, excellent family recreation, low housing costs, with both urban and rural life-styles. Contact Dr Donn Cobb, Health Officer, Fresno County Dept of Health, PO Box 11867, Fresno, CA 93775; (209) 445-3202.

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COLORADO, WASHINGTON, NORTHERN CALIFORNIA. Exceptional practice opportunities now available in Family Practice, Pediatrics, Internal Medicine, Psychiatry, and OB. Send CV to D. A. Franklin, MD, and Associates, 4894 Sterling Dr, Boulder, CO 80301.

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SUBSTANCE ABUSE—CHEMICAL DEPENDENCE. Ten years experience including acute care and patient education. BC Internist medeligible for AMSAOD exam. Current location, southern California. Reply to Number 167, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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(Continued on Page 367)

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NORTHERN AND CENTRAL CALIFORNIA

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BERKELEY, CALIFORNIA, FAMILY PRACTICE. 10 years established, including fully equipped medical office. Option to buy part of building available. Attractive financing terms. Send letter and résumé to Number 166, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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Ads Get Results!

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MEDICAL EQUIPMENT

FOR SALE. Circadian Holter Monitor—Reichert colonoscope 65 cm, all attachments. Leslie M. Morrisset, MD, 1208 N. 2nd St, El Cajon, CA 92021; (619) 442-2909.

MEETINGS

SEVENTH ANNUAL ADVANCES IN HEART DISEASE
December 1-3, 1989, San Francisco, California. Fees: $350 for ACC members; $415 for non-members; $175 for residents, fellows-in-training, nurses, and technicians. 19 Category 1 credit hours. For information, call **American College of Cardiology, (800) 253-4636; in Maryland, (301) 897-5400.**

COURSES

KAUAI, HAWAII, JANUARY 20-28, 1990
TWO CONTINUING EDUCATION PROGRAMS FOR GENERALISTS AND INTERNISTS
Family Practice: Caring and Curing, January 20-25. Pain Management: Compleat Approach, January 26-28. Contact **Academy for Continuing Education of Kauai, PO Box 457, Kalaheo, HI 96741.**

ST PAUL'S HOSPITAL CME COURSE, Vancouver, November 1, 2, 3, 1989. The 35th Annual St Paul's Hospital Continuing Medical Education Course will be held at the Vancouver Convention Centre. This popular course is directed to Family Physicians in both rural and urban practices and will provide excellent speakers on Back Pain; Hyperlipidemia; Emergency; Therapeutics; AIDS; Eyes/ENT. For further information: Susan Tate-Smith, Medical Services, St Paul's Hospital, 1081 Burrard St, Vancouver, BC V6Z 1Y6, Canada; (604) 682-2344, loc 2721.

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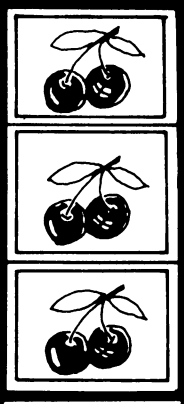

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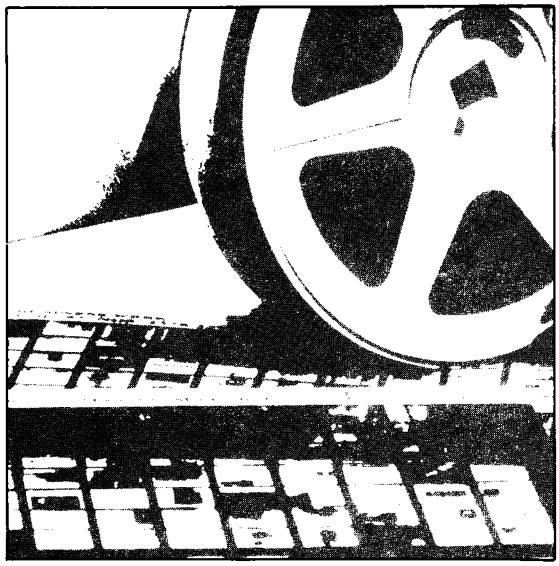

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In active duodenal ulcers

Once-a-night h.s. therapy controls acid rain

Zantac 300
ranitidine HCl Glaxo

ZANTAC® 150 Tablets
(ranitidine hydrochloride)
ZANTAC® 300 Tablets
(ranitidine hydrochloride)

BRIEF SUMMARY

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:
1. Short-term treatment of **active duodenal ulcer**. Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer**. Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD)**. Symptomatic relief commonly occurs within one or two weeks after starting therapy. Therapy for longer than six weeks has not been studied.

In active duodenal ulcer; active, benign gastric ulcer; hypersecretory states; and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: General: 1. Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.
2. Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

Laboratory Tests: False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy, and therefore testing with sulfosalicylic acid is recommended.

Drug Interactions: Although ZANTAC has been reported to bind weakly to cytochrome P-450 in vitro, recommended doses of the drug do not inhibit the action of the cytochrome P-450-linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in lifespan studies in mice and rats at doses up to 2,000 mg/kg/day.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella, E coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg to male rats was without effect on the outcome of two matings per week for the next nine weeks.

Pregnancy: *Teratogenic Effects: Pregnancy Category B:* Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to ZANTAC. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: ZANTAC is secreted in human milk. Caution should be exercised when ZANTAC is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Use in Elderly Patients: Ulcer healing rates in elderly patients (65 to 82 years of age) were no different from those in younger age groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age groups.

ADVERSE REACTIONS: The following have been reported as events in clinical trials or in the routine management of patients treated with oral ZANTAC®. The relationship to ZANTAC therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to ZANTAC administration.

Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported.

Cardiovascular: Rare reports of tachycardia, bradycardia, and premature ventricular beats.

Gastrointestinal: Constipation, diarrhea, nausea vomiting, and abdominal discomfort/pain.

Hepatic: In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid IV for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

Musculoskeletal: Rare reports of arthralgias.

Hematologic: Reversible blood count changes (leukopenia, granulocytopenia, thrombocytopenia) have occurred in a few patients. Rare cases of agranulocytosis or of pancytopenia, sometimes with marrow hypoplasia, have been reported.

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by ZANTAC® (ranitidine hydrochloride) and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when ZANTAC has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Integumentary: Rash, including rare cases suggestive of mild erythema multiforme, and rarely, alopecia.

Other: Rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC® 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

August 1987

Glaxo

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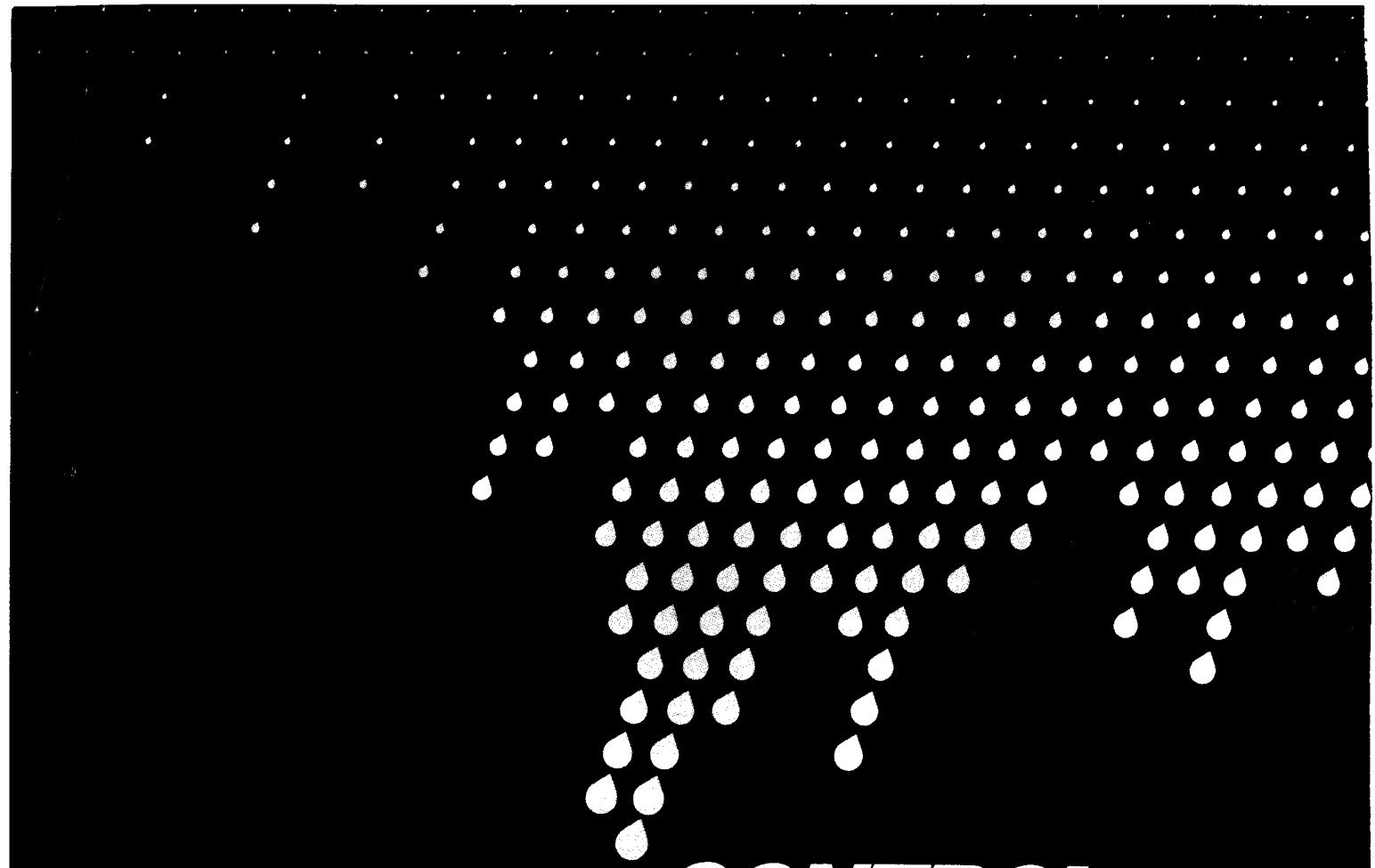

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